

Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)
National Institutes of Health ([NIH \(http://www.nih.gov\)](http://www.nih.gov))

Components of Participating Organizations
NATIONAL CANCER INSTITUTE ([NCI \({issuingComponent.orgLink}\)](#))

Note: Not all NIH Institutes, Centers, and Offices (ICOs) participate in Announcements. Applicants should carefully note which ICOs participate in this announcement and view their respective areas of research interest at the [ICO-Specific Scientific Interests website \(https://grants.nih.gov/funding/find-a-fit-for-your-research/nih-institutes-centers-offices\)](https://grants.nih.gov/funding/find-a-fit-for-your-research/nih-institutes-centers-offices). ICOs that do not participate in this announcement will not consider applications for funding.

Funding Opportunity Title
Pancreatic Cancer Detection Consortium: Research Units (U01 Clinical Trial Optional)

Activity Code
[U01 \(http://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=u01&Search.x=0&Search.y=0&Search_Type=Activity\)](http://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=u01&Search.x=0&Search.y=0&Search_Type=Activity) Research Project – Cooperative Agreements

Announcement Type
Reissue of PAR-21-334

Related Notices

- Check for any recent [Notices of NIH Policy Changes \(https://grants.nih.gov/grants/guide/url_redirect.php?id=11163\)](https://grants.nih.gov/grants/guide/url_redirect.php?id=11163) that may impact application requirements.

Funding Opportunity Number (FON)
PAR-28-056

Companion Funding Opportunity
[PAR-28-057 \(https://www.grants.gov/search-results-detail/361276\)](https://www.grants.gov/search-results-detail/361276), [U24 \(https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=U24&&Search.x=0&&Search.y=0&&Search_Type=Activity\)](https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=U24&&Search.x=0&&Search.y=0&&Search_Type=Activity) Resource-Related Research Project (Cooperative Agreements)

Number of Applications
See Section III. 3. Additional Information on Eligibility.

Assistance Listing Number(s)
93.393

Funding Opportunity Purpose
Through this Notice of Funding Opportunity (NOFO), NCI solicits applications for the Research Units (RUs), one of the two scientific components of the Pancreatic Cancer Detection Consortium (PCDC), to conduct research on early detection of pancreatic ductal adenocarcinoma (PDAC) and characterization of its precursor lesions to identify patients who are at high risk of progression to cancer. The PCDC will continue to address one of the four research priorities identified in the NCI's 2014 Scientific Framework for Pancreatic Ductal Adenocarcinoma (PDAC). The PCDC will support research for the development and testing of new molecular and imaging biomarkers for detecting PDAC early and for identifying patients at high risk of PDAC (because of genetic factors, family history and/or the presence of precursor lesions) who could be candidates for early intervention.

The PCDC-RUs will consist of multi-disciplinary teams and will undertake studies to: identify and test biomarkers measurable in bodily fluids for early detection of PDAC and/or its precursor lesions; develop molecular- and/or imaging-based markers of pancreatic cysts and determine which lesions are likely to progress to cancer; develop molecular- and/or imaging-based approaches for screening populations at high risk of PDAC; use machine learning and computational approaches towards biomarker discovery and/or validation; and conduct biomarker validation studies. The PCDC-RUs will also collect longitudinal biospecimens for building a biorepository. Each PCDC-RU is expected to participate in collaborative activities with other PCDC-RUs and share ideas, biospecimens, and data within the Consortium.

Funding Opportunity Goal(s)
To identify cancer risks and risk reduction strategies, to identify factors that cause cancer in humans, and to discover and develop mechanisms for cancer prevention and preventive interventions in humans.

Key Dates

Posted Date

Open Date (Earliest Submission Date)

January 05, 2027

The following table includes NIH [standard due dates \(https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/due-dates.htm\)](https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/due-dates.htm) marked with an asterisk.

Application Due Dates			Review and Award Cycles		
New	Renewal / Resubmission / Revision (as allowed)	AIDS - New/Renewal/Resubmission/Revision, as allowed	Scientific Merit Review	Advisory Council Review	Earliest Start Date
February 05, 2027 *	March 05, 2027 *	Not Applicable	July 2027	October 2027	December 2027
June 05, 2027 *	July 05, 2027 *	Not Applicable	November 2027	January 2028	April 2028
October 05, 2027 *	November 05, 2027 *	Not Applicable	March 2028	May 2028	July 2028
February 05, 2028 *	March 05, 2028 *	Not Applicable	July 2028	October 2028	December 2028
June 05, 2028 *	July 05, 2028 *	Not Applicable	November 2028	January 2029	April 2029
October 05, 2028 *	November 05, 2028 *	Not Applicable	March 2029	May 2029	July 2029
February 05, 2029 *	March 05, 2029 *	Not Applicable	July 2029	October 2029	December 2029
June 05, 2029 *	July 05, 2029 *	Not Applicable	November 2029	January 2030	April 2030
October 05, 2029 *	November 05, 2029 *	Not Applicable	March 2030	May 2030	July 2030

All applications are due by 5:00 PM local time of applicant organization.

Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

Due Dates for E.O. 12372

Not Applicable

Expiration Date

November 06, 2029

Required Application Instructions

It is critical that applicants follow the instructions in the Research (R) Instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400), except where instructed to do otherwise (in this NOFO or in a Notice from [NIH Guide for Grants and Contracts \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164)).

Conformance to all requirements (both in the Application Guide and the NOFO) is required and strictly enforced. Applicants must read and follow all application instructions in the Application Guide as well as any program-specific instructions noted in Section IV. When the program-specific instructions deviate from those in the Application Guide, follow the program-specific instructions.

Applications that do not comply with these instructions may be delayed or not accepted for review.

There are several options available to submit your application through Grants.gov to NIH and Department of Health and Human Services partners. You **must** use one of these submission options to access the application forms for this opportunity.

1. Use the [NIH ASSIST system \(https://public.era.nih.gov/assist/landing_era?tblId=0819b5fc-46b7-4f02-b6b7-127e5a4e19fa\)](https://public.era.nih.gov/assist/landing_era?tblId=0819b5fc-46b7-4f02-b6b7-127e5a4e19fa) to prepare, submit and track your application online.
2. Use an institutional system-to-system (S2S) solution to prepare and submit your application to Grants.gov and [eRA Commons \(https://public.era.nih.gov/commons/\)](https://public.era.nih.gov/commons/) to track your application. Check with your institutional officials regarding availability.
3. Use [Grants.gov \(https://grants.gov/search-grants?oppStatuses=closed|archived|posted|forecasted&fon=PA-25-301\)](https://grants.gov/search-grants?oppStatuses=closed|archived|posted|forecasted&fon=PA-25-301) Workspace to prepare and submit your application and [eRA Commons \(http://public.era.nih.gov/commons/\)](http://public.era.nih.gov/commons/) to track your application.

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Part 2. Full Text of Announcement

Section I. Notice of Funding Opportunity Description

Background

Pancreatic Cancer: Pancreatic cancer is the third leading cause of cancer-related mortality in the United States and is projected to move up to the second position by 2030. The poor prognosis of pancreatic cancer is primarily due to the diagnosis of the disease at advanced stages as patients often present with locally advanced or metastatic disease where resection is not feasible. The lack of symptoms or presence of non-specific symptoms at early stages makes it challenging to detect this cancer early. However, early detection significantly improves survival outcomes. Surgical resection remains the only potentially curative treatment, but only approximately 20% of patients are eligible for surgery at diagnosis. Even among those who undergo surgery, the recurrence rate is still high.

PCDC was initiated as a consequence of the Recalcitrant Cancer Research Act of 2012 and the NCI 2014 Scientific Framework for Pancreatic Ductal Adenocarcinoma. Pancreatic cancer has a 5-year relative survival rate of 13.3%, with an estimated 67,440 new cases, and 51,980 deaths in the United States in 2025 (SEER)

The majority of PDAC is sporadic, i.e., occurring without a family history or a genetic predisposition of the disease. It is estimated that it takes more than 10 years before an initiating mutation in a normal pancreas cell progresses to the non-metastatic parental founder cell of PDAC, and at least five more years may be required for the acquisition of metastatic ability. This window of time offers an opportunity for curative interventions if the disease could be diagnosed at an earlier stage. Evidence suggests that once PDAC becomes detectable, the clinical progression from early-stage to advanced-stage disease is rapid; therefore, the best outcomes will be tied with detection at the earliest stages of the disease.

Liquid biopsy approaches specific to PDAC, including assays based on ctDNA, methylation signatures, exosomal RNA, and protein biomarkers are actively being explored by PCDC for biomarkers that will predict progression of pre-cancer lesions and/or detect early stage PDAC in high risk populations. PCDC is also integrating imaging approaches with liquid biopsies for PDAC detection. However, there remains a need for the development and validation of better molecular, imaging and/or integrated molecular and imaging approaches that are highly discriminating for pancreatic cancer and clinically useful.

Biomarker Definition. In the context of this NOFO, biomarkers are defined as cellular, morphological, biochemical, molecular, histological, and imaging (molecular or radiographic) characteristics by which normal and/or abnormal biological processes can be recognized and/or monitored. Biomarkers are measurable in biological materials, such as, in tissues, cells, and/or bodily fluids.

Current PCDC Overview: Currently available modalities for screening those at high risk of pancreatic cancer are mostly anatomical imaging methods, including traditional cross-sectional imaging such as abdominal ultrasound or computed tomography (CT). For surveillance imaging protocols include magnetic resonance imaging (MRI)/magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasound (EUS), or CT when MRI and EUS are not possible. Traditional cross-sectional imaging has limited sensitivity for detecting very early pancreatic cancer and its microscopic precursor lesions. The consortium is developing several clinically useful screening markers that should be present in those patients with high-grade precursor lesions (intraductal papillary mucinous neoplasm [IPMN], mucinous cystic neoplasm [MCN], and pancreatic intraepithelial neoplasia-grade 3 [PanIN-3]) and early-stage PDAC, while absent in those without neoplasia, such as pancreatitis. PCDC is also working with the Early Detection Research Network (EDRN) and the Alliance of Pancreatic Cancer Consortia (APaCC) to develop a repository of pre-cancer images that are available for developing and validating artificial intelligence (AI)-based algorithms to identify pre-cancer in CT scans.

The PCDC currently focuses on two main types of high-risk populations that are outlined below:

- (1) Individuals at high risk of developing PDAC because of genetic factors, i.e., presence of germline variants in cancer susceptibility genes that include high-penetrance genes (such as *BRCA2*, *STK11/LKB1*, *CDKN2A*, *PALB2*), hereditary pancreatitis (*PRSS1* mutation carriers), and other known variants. Individuals could also be at high risk of PDAC due to a family history of pancreatic cancer. Approximately 10% of PDAC occurs in families with a history of PDAC.
- (2) Individuals at high risk of developing PDAC because of the presence of mucinous cyst lesions (e.g., IPMN and MCN), and other suspected precursors such as PanIN-3. IPMNs and MCNs are being increasingly detected because of increased abdominal imaging such as CT done for diagnostic workup of non-specific symptoms. An estimated 15% of PDAC originate from these lesions, but their natural history is not well-defined. Advancements in metabolic and other molecular imaging technologies have started to show promise and potential for future clinical use.

Multi-cancer detection (MCD) tests are blood-based assays designed to identify multiple cancers at early, more treatable stages by detecting tumor-derived signals such as ctDNA, DNA methylation patterns, and protein biomarkers using similar technology that PCDC is using for PDAC detection. Key challenges for MCDs include the inability to detect preinvasive lesions and early stage PDAC. PCDC is focused on developing and validating more sensitive assays that could be useful for screening MCD test positive patients.

PCDC Research Focus: The PCDC objectives include the development of tests with high clinical sensitivity and specificity that can accurately detect progressive precursors and early-stage PDAC in noninvasively or minimally invasively obtained biospecimens. High specificity for these tests is particularly important, since a positive test may trigger invasive procedures. In addition, these tests must be rapid, cost-effective, widely distributable, and designed with practical in real-world settings. Since biomarkers alone may not provide sufficient tissue specificity. The PCDC research focus includes the development of biomarkers in conjunction with imaging modalities (including radiographic, metabolic and molecular imaging techniques).

The PCDC follows the same biomarker development principles established by the EDRN, where the five phases for biomarker discovery and validation were defined as:

- Phase 1: The preclinical exploratory phase;
- Phase 2: The clinical assay validation phase (case-control);
- Phase 3: The retrospective longitudinal validation phase;
- Phase 4: The prospective screening phase; and
- Phase 5: The cancer control phase.

The articles on the five-phase approach and PRoBE study design are available on the EDRN website.

PCDC Resource Building Efforts: A major impediment to pancreatic cancer research is the limited access to well-characterized and well-annotated specimens from early stages and lethal precursors, which are critical for biomarker discovery and validation. PCDC has initiated the establishment of comprehensive, longitudinal registries and biorepositories, a necessary and foundational step toward advancing early detection strategies. Pancreatic cancer is often diagnosed at late stages and the rapid progression and high mortality of PDAC make it difficult to obtain high-quality biospecimens, particularly from early-stage patients. Another shortcoming in the field is the inability of investigators to fully utilize the existing resources of individual facilities across institutions, which limits collaboration and reduces the efficiency of existing efforts. Registries and cohorts of patients at high risk of PDAC seldom have pre-diagnostic specimens and very few have serial/longitudinal samples, which are essential for identifying dynamic biomarkers that reflect disease initiation and progression.

PCDC is addressing these challenges by building two integrated, longitudinal biorepositories. Samples that have already been collected under ongoing PCDC activities are being shipped to a Central Repository for long-term storage. The use of these precious samples for EDRN-defined Phase 3 biomarker validation studies will follow established consortium and NCI review and access processes. The full engagement and collaboration from PCDC investigators in building these shared resources, which are critical for achieving the Consortium's goals and accelerating progress in early detection research for the broader scientific community is required.

PCDC Prospective Cohorts: This is a unique, ongoing collection of prospective, longitudinal biospecimens including blood [serum, plasma], cyst fluid, and pancreatic juice from the types of high-risk populations previously described. These cohorts known as "PCDC Prospective Cohorts", are being developed through strong multi-institutional collaborations across all PCDC grant recipients. The collection of sufficient biospecimens that will enable the design of adequately powered, EDRN-defined Phase 3 validation studies will require continued commitment and strong collaborations among multiple institutions and participating Cancer Centers.

PCDC Reference Sets: The PCDC teams are also prospectively collecting blood samples from consented participants who have the following conditions:

- PDAC;
- Pancreatic cyst;
- Pancreatitis;
- Other pancreatic cancer;
- Familial/genetic risk;
- New onset diabetes (NOD);
- Non-PDAC control.

These biospecimens are designated as reference sets for various larger validation projects, within PCDC or with other NCI-funded consortia.

Applications Not Responsive to this NOFO

The following types of studies are not responsive to this NOFO. Applications proposing such studies will be considered non-responsive and will not be reviewed or considered for funding:

- Research on new genome-wide association studies (GWAS), mechanistic or basic research (i.e., growth regulation, cell cycle control) or investigations that are not explicitly focused on detection of early-stage PDAC or risk assessment of its precursor lesions in humans.
- Studies focused exclusively on *in silico* approaches or those proposing only the development of risk prediction models without clinical validation.
- Studies based exclusively on preclinical models (e.g., mouse, organoid) are not acceptable, and all applications must include human subjects.
- Studies based exclusively or predominantly on the discovery of new biomarkers are not acceptable. All studies must include clinical validation studies.

Investigators proposing NIH-defined clinical trials may refer to the [Research Methods Resources \(http://grants.nih.gov/grants/guide/url_redirect.php?id=82448\)](http://grants.nih.gov/grants/guide/url_redirect.php?id=82448) website for information about developing statistical methods and study designs.

See Section VIII. Other Information for award authorities and regulations.

Section II. Award Information

Funding Instrument

Cooperative Agreement: A financial assistance mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, NIH scientific or program staff will assist, guide, coordinate, or participate in project activities. See Section VI.2 for additional information about the substantial involvement for this NOFO.

Application Types Allowed

New
Renewal
Resubmission
Revision

The [OER Glossary \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11116\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11116) and the How to Apply Application Guide provide details on these application types. Only those application types listed here are allowed for this NOFO.

Clinical Trial?

Optional: Accepting applications that either propose or do not propose clinical trial(s).

[Need help determining whether you are doing a clinical trial? \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82370\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82370)

Funds Available and Anticipated Number of Awards

The number of awards is contingent upon NIH appropriations and the submission of a sufficient number of meritorious applications.

Award Budget

Application budget should not exceed \$600K direct costs per year and need to reflect the actual needs of the proposed project.

Award Project Period

The project period is 5 years.

NIH grants policies as described in the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120) will apply to the applications submitted and awards made from this NOFO.

Section III. Eligibility Information

1. Eligible Applicants

Eligible Organizations

Higher Education Institutions - Includes all types

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

Nonprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

For-Profit Organizations

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

Local Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribal Governments (Other than Federally Recognized).

Federal Governments

- Eligible Agencies of the Federal Government
- U.S. Territory or Possession

Other

- Independent School Districts
- Public Housing Authorities/Indian Housing Authorities
- Native American Tribal Organizations (other than Federally recognized tribal governments)
- Faith-based or Community-based Organizations
- Regional Organizations

Foreign Organizations/International Collaborations

Non-domestic (non-U.S.) Entities (Foreign Organizations) **are not** eligible to apply.

Non-domestic (non-U.S.) components of U.S. Organizations **are not** eligible to apply.

Foreign components, as [defined in the NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11118\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11118), **are not** allowed.

Required Registrations

Applicant Organizations

Applicant organizations must complete and maintain the following registrations as described in the How to Apply- Application Guide to be eligible to apply for or receive an award. All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or more, so applicants should begin the registration process as soon as possible. Failure to complete registrations in advance of a due date is not a valid reason for a late submission, please reference the [NIH Grants Policy Statement Section 2.3.9.2 Electronically Submitted Applications \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=82423\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82423) for additional information.

- [System for Award Management \(SAM\) \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82390\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82390) – Applicants must complete and maintain an active registration, **which requires renewal at least annually**. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code. Foreign organizations must obtain a [NATO Commercial and Government Entity \(NCAGE\) Code \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11176\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11176) (in lieu of a CAGE code) in order to register in SAM.
 - Unique Entity Identifier (UEI)- A UEI is issued as part of the SAM.gov registration process. The same UEI must be used for all registrations, as well as on the grant application.
- [eRA Commons \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=11123\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=11123) - Once the unique organization identifier is established, organizations can register with eRA Commons in tandem with completing their Grants.gov registrations; all registrations must be in place by time of submission. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.
- [Grants.gov \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=82300\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82300) – Applicants must have an active SAM registration in order to complete the Grants.gov registration.

Program Directors/Principal Investigators (PD(s)/PI(s))

All PD(s)/PI(s) must have an eRA Commons account. PD(s)/PI(s) should work with their organizational officials to either create a new account or to affiliate their existing account with the applicant organization in eRA Commons. If the PD/PI is also the organizational Signing Official, they must have two distinct eRA Commons accounts, one for each role. Obtaining an eRA Commons account can take up to 2 weeks.

All PD(s)/PI(s) must be registered with [ORCID \(https://orcid.org/\)](https://orcid.org/). The personal profile associated with the PD(s)/PI(s) eRA Commons account must be linked to a valid ORCID ID. For more information on linking an ORCID ID to an eRA Commons personal profile see the [ORCID topic in our eRA Commons online help \(https://era.nih.gov/erahelp/Commons/default.htm#orcid.htm%3FTocPath%3D____29\)](https://era.nih.gov/erahelp/Commons/default.htm#orcid.htm%3FTocPath%3D____29).

Eligible Individuals (Program Director/Principal Investigator)

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)) is invited to work with their organization to develop an application for support.

For institutions/organizations proposing multiple PDs/PIs, visit the Multiple Program Director/Principal Investigator Policy and submission details in the Senior/Key Person Profile (Expanded) Component of the How to Apply-Application Guide.

An investigator designated as a Contact PD/PI or MPI for a PCDC-RU application must not be the designated Contact PD/PI or MPI of another application under this NOFO, under the companion U24 NOFO, [PAR-28-057 \(https://public.era.nih.gov/foa/#/announcements/dashboard?foaId=30804\)](https://public.era.nih.gov/foa/#/announcements/dashboard?foaId=30804) or any currently funded RUs.

2. Cost Sharing

This NOFO does not require cost sharing as defined in the [NIH Grants Policy Statement Section 1.2 Definition of Terms \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11126\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11126).

3. Additional Information on Eligibility

Number of Applications

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

The NIH will not accept duplicate or highly overlapping applications under review at the same time, per [NIH Grants Policy Statement Section 2.3.7.4 Submission of Resubmission Application \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82415\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82415). This means that the NIH will not accept:

- A new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.
- A resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.
- An application that has substantial overlap with another application pending appeal of initial peer review (see [NIH Grants Policy Statement 2.3.9.4 Similar, Essentially Identical, or Identical Applications \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82423\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82423)).

Section IV. Application and Submission Information

1. Requesting an Application Package

The application forms package specific to this opportunity must be accessed through ASSIST, Grants.gov Workspace or an institutional system-to-system solution. Links to apply using ASSIST or Grants.gov Workspace are available in Part 1 of this NOFO. See your administrative office for instructions if you plan to use an institutional system-to-system solution.

2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the Research (R) Instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) except where instructed in this notice of funding opportunity to do otherwise (in this NOFO, in a [policy notice \(https://grants.nih.gov/grants/guide/uri_redirect.php?id=11163\)](https://grants.nih.gov/grants/guide/uri_redirect.php?id=11163), or other notice from [NIH Guide for Grants and Contracts \(https://grants.nih.gov/grants/guide/uri_redirect.php?id=11164\)](https://grants.nih.gov/grants/guide/uri_redirect.php?id=11164)). Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review.

Page Limitations

All page limitations described in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/how-to-apply-application-guide.html\)](https://grants.nih.gov/grants/how-to-apply-application-guide.html) and the [Table of Page Limits \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=61134\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=61134) must be followed.

Instructions for Application Submission

The following section supplements the instructions found in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/how-to-apply-application-guide.html\)](https://grants.nih.gov/grants/how-to-apply-application-guide.html) and should be used for preparing an application to this NOFO.

SF424(R&R) Cover

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed.

SF424(R&R) Project/Performance Site Locations

All instructions in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed.

SF424(R&R) Other Project Information

All instructions in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed.

SF424(R&R) Senior/Key Person Profile

All instructions in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed.

R&R or Modular Budget

All instructions in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed.

- *PD(s)/PI(s) Effort*: The Contact PD/PI must commit a minimum of 1.2 person-month of his/her time per year. For multi-PD/PI applications, the Contact PD/PI and all other PDs/Pis must commit a minimum of 1.2 person-month of their time per year to the award. This commitment cannot be reduced in later years of the award.
- *Set-Aside Funds for Trans-PCDC Projects*: For years 2-5, applicants must set aside \$100,000 (direct cost) of their annual budget for PCDC collaborative studies. The set-aside amount should be presented in the "Other Direct Costs" category under the heading "Consortium Collaborative Funds". The use of the set-aside funds will be restricted for trans-PCDC collaborative studies developed post-award. A major portion of the restricted set-aside funds will be used to support the biospecimen collections for the PCDC Prospective Cohorts. The collaborative studies will be subject to review and recommendation for approval by the Steering Committee. The NCI authorization to use these restricted funds will be contingent upon the recommendation of the Steering Committee.
- *Single Institutional Review Board (sIRB)*: Applicants should account for sIRB expenses, if applicable to the proposed study.
- *Support for Early-stage/Junior Investigators*: The budget should include funds to enhance professional development of early-stage/junior investigators. The budget should include funds to cover their participation in research projects.
- *Travel Funds*: Applicants must budget for travel and per diem expenses for Steering Committee meetings. The Contact PD/PI together with at least one MPI or a senior investigator and an early-stage/junior investigator will attend two Steering Committee meetings each year of the award; one in-person meeting and one virtual meeting. The virtual meetings will allow participation of the larger team members.
- *NOTE*: Recipient-selected projects that involve clinical trials or studies involving greater than minimal risk to human subjects require approval by NIH prior to initiation. The grant recipient will comply with the NIH Guidance on Changes That Involve Human Subjects in Active Awards and That Will Require Prior NIH Approval. The grant recipient will provide NIH with specific plans for data and safety monitoring, and will notify the IRB and NIH of serious adverse events and unanticipated problems, consistent with NIH Data and Safety Monitoring Plan policies.

R&R Subaward Budget

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed.

PHS 398 Cover Page Supplement

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed.

PHS 398 Research Plan

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed, with the following additional instructions:

Specific Aims: In addition to the specific aims, applicants must include the relevance of the research to the objectives of this NOFO.

Research Strategy: Applicants must organize the Research Strategy to include the sub-section elements identified below. Applicants may include other sub-sections as needed.

Sub-section A: Overview of Research Strategy

Outline the overall theme of the proposed research, as well as the significance and innovation of the proposed studies. Propose research on the identification and testing of biomarkers measurable in bodily fluids for early detection of PDAC or its precursor lesions; determine which pancreatic cysts are likely to progress to cancer; develop molecular- and/or imaging-

based approaches for screening populations at high risk of PDAC; conduct biomarker validation studies; and collect biospecimens for the establishment of bio-repositories (PCDC Prospective Cohorts and Reference Sets).

Define during the initial phases of development the intended clinical context in which a biomarker test will be used and the likelihood of its use in routine clinical practice, if shown to be efficacious.

For research on biomarkers, applicants are encouraged to incorporate the five-phase biomarker development approach. This approach is used for successfully translating research on biomarker applications from the laboratory to the bedside.

Sub-section B: Research Approaches

It is essential that each PCDC-RU identifies and concentrates resources on the most promising scientific opportunities, completes studies as planned, employs sound methodologies, and, where appropriate, be innovative. The proposed research approach must include one or more of the following strategies.

- Development and validation of 'omic'-based assays to detect early-stage PDAC, PanIN-3, high-grade IPMN, and MCN;
- Use of retrospective, cross-sectional, case-control cohorts to determine the sensitivity and specificity of a defined biomarker or biomarker panel in clinically appropriate populations (EDRN-defined Phase 2 study, specimens collected from case patients at the time of diagnosis);
- Determine the sensitivity and specificity of a defined biomarker or biomarker panel to detect preclinical disease;
- Conduct analytical studies, including inter- and intra-laboratory assessments, to establish and compare the sensitivity and specificity as well as the predictive accuracy of biomarkers in a clinical context;
- Use data science approaches for the analysis, integration, and interpretation of experimental data (genomics, proteomics, metabolomics, imaging etc.);
- Determine the accuracy of a biomarker or a panel of biomarkers to predict progression from a precancerous lesion to cancer (e.g., use longitudinal biospecimens and images from patients with pancreatic cysts to determine those lesions that are likely to progress to adenocarcinoma within a defined period and determine which cysts have high malignant potential);
- Determine the accuracy of biomarkers to predict the extent or severity of disease;
- Perform comprehensive studies in targeted, high-risk populations for validation and potential integration of novel detection strategies;
- Development of new imaging (molecular or radiographic) modalities to detect high-risk precursor lesions that are currently radiographically occult (e.g., PanIN-3);
- Integration of imaging and molecular markers to detect early-stage PDAC and PanIN-3 or to predict progression from IPMNs or MCNs to PDAC;
- Development of novel methods to obtain and interrogate biospecimens (e.g., study duct cancerization);
- Development of more accurate and sensitive imaging methods to detect early-stage PDAC, PanIN-3, IPMN or MCN that add to existing clinical management/standard of care and could be used to select patients for surgical intervention;
- Development and integration of imaging approaches and multiplexed marker panels; and
- Development of artificial intelligence/deep learning/machine learning language approaches for mining big data, including imaging data.

Sub-section C: Study Design

The proposed study may initially involve the analysis of biospecimens from patients with neoplastic lesions vs. respective control biospecimens (case-control or cohort samples) and with adequate follow-up information. A study may involve the use of retrospectively identified and/or prospectively collected specimens. Applicants must describe in detail any proposed retrospective (existing) and/or prospective specimen collections that will be used for PCDC collaborative activities. The description must include information on the types of patients and control subjects to be accrued, clinical information to be collected, types of specimens to be collected, and quality control of the biospecimens.

Applicants must define and describe detailed eligibility criteria in reference to incidental screening of high-risk cohorts, or symptom detected settings. If there is a deviation from this mode of detection, such as using a questionnaire in a face-to-face interview to collect demographics and mode of detection information, applicants must describe the process. Applicants must include details of how the ascertainties were made for screen-detected or symptom-detected cases. If using retrospective cohorts, criteria for eligibility and cohort details must be provided along with detailed clinical information, such as data on follow-up, which endpoints were ascertained (cancer progression, death, cause of death) and how the endpoints were ascertained; patient age; disease stage; tumor size; lymph node status; and any other relevant diagnosis and treatment details. In situations where the specimens are being assembled from different sources and populations in terms of geography, demographics, etc., applicants must address the possibility of potential biases in the study design and take measures to minimize such biases.

Applicants must include a clear statement on how statistical power is defined for multiple tests and the sample size that is required to achieve this power. Examples of power definition include (a) the probability to detect at least one of possible true non-zero effects; (b) the probability to detect all non-zero effects; and (c) the true discovery rate, etc. Also, in case-control designs, applicants must provide clear descriptions of whether matching is involved and what confounders are adjusted for and why.

Applicants should consider the following guidelines to avoid bias and make the best use of resources starting with the discovery process:

- Proposed biomarker validation studies should follow the principles of the PRoBE study design (Pepe et al., J Natl Cancer Inst. 2001) or a similar study design;
- Discovery studies should use key elements of the PRoBE design, including a randomized selection of case patients and control subjects from a well-defined prospective cohort that is relevant to the intended clinical application;
- Use of rigorous protocols that precisely define data items and procedures to measure them, and mechanisms to ensure that biomarker and outcome assessments cannot influence each other;
- Wherever possible, an evaluation study should be conducted for biomarkers that show promise in discovery studies that use the same clinical context and population; the evaluation of the performance of a marker or marker combination can be undertaken by using a PRoBE design and randomly splitting the dataset into a training set for discovery and a test set for evaluation.

Applicants must describe the infrastructure for data storage, data security and data analysis.

Sub-section D: Relevant Accomplishments

Relevant Recent Accomplishments (All Applicants): Applicants must provide, without duplicating information provided in the biosketches, a brief description of previous research experience and accomplishments relevant to the development of biomarkers and/or imaging methods for early detection of pancreatic cancer, as well as biospecimen collection.

Progress Report (Renewal Applicants Only): Applicants must include additional information in this section summarizing the current 5-year funding period and include the following items (a to d):

- List the specific aims from previously funded application. Describe the progress made relevant to these specific aims during the current funding period and highlight the key findings for the biomarkers investigated.
- Indicate the status of the developed markers based on the EDRN-defined biomarker development phases. Included the steps taken to advance biomarkers to Phase 2 and/or Phase 3 validation? For any unsuccessful discovery efforts, describe the alternative approaches that can be taken in the present application to be more effective. For biomarkers that have been eliminated from further investigation, briefly explain the reasons for that decision.
- Describe the progress made on biomarker research supported through the restricted set-aside funds, if set-aside funds were used for this purpose.
- Describe patient accrual and biospecimen contribution towards the PCDC Prospective Cohorts and/or towards building the case-control Reference Sets.

*Sub-section E: PCDC Collaborative Responsibilities*Building Biorepositories

Applicants must document their capabilities regarding access to patients at high risk of PDAC (e.g., familial and hereditary registries, presence of IPMN and MCN), recruitment of patients, procurement of biospecimens prospectively and longitudinally, collection of epidemiological and clinical data using CDEs, protocol development, pathological assessment, biospecimen quality control, as well as the ability to process, track, store and ship specimens. Applicants are encouraged to collaborate with Cancer Centers and/or cooperative groups for any appropriate ongoing trials and/or surveillance cohorts for access to suitable patient populations and any unique opportunity for prospective longitudinal collection of specimens.

Applicants must also document their ability to collect cross-sectional biospecimens from sporadic cases of early-stage PDAC (stages IA, IB, IIA, and IIB) and any other histological type, pancreatic cancer precursor lesions (PanINs), cystic lesions (IPMNs and MCNs), and benign pancreatic conditions (e.g., chronic pancreatitis, biliary obstruction). Types of biospecimens to be collected may include plasma, serum, buffy coat, DNA, stool, urine, pancreatic juice, cyst fluid, diagnostic tissue biopsies, pancreatic resections, image-guided proximal samples (e.g., EUS guided). Applicants with the ability to collect autopsy samples (precursor and early-stage cases) should include procedures for acquiring samples and obtain/submit clearances from state and regulatory authorities, including those from an institutional review board (IRB).

Applicants must describe plans for depositing a portion of the samples collected during the tenure of this funding in the NCI at Frederick Central Repository for building the PCDC Prospective Cohorts and the Reference Sets (cases and controls) described earlier. The PCDC-RUs are expected to coordinate with the PCDC-MDCU for trans-PCDC collaborative projects, protocol development, statistical analyses, biospecimen blinding, biospecimen data deposition supported by the PCDC-MDCU, and for tracking, shipping, and storing biospecimens at the NCI at Frederick Central Repository. New applicants must note that biospecimen collection for the PCDC Prospective Cohorts will be mainly based on the SOPs and CDEs already established by the current PCDC and approved by the Steering Committee.

Joint Collaborative Activities

All awardees will be required to interact closely with each other, engage in collaborative activities, and share resources, data, ideas and expertise that are beyond the scope of a single research team. For the Prospective Cohorts, the RUs are required to follow the protocols/standard operating procedures (SOPs) and common data elements (CDEs) that have already been established by the current PCDC teams. Funding could be delayed if institutes are not able to agree to these requirements. The NCI also encourages prospective collection of pre-diagnostic images for the development of AI-based tools/methods.

Investigators are required to devote a portion of their effort to participate in trans-PCDC collaborative activities post-Award. Restricted funds will be used for these activities (see R&R Budget section) and will commence in year 2 after receiving the PCDC Steering Committee (defined below) recommendation for approval. Awardees will be charged with developing collaborative projects, resources for the community, and outreach activities. Applicants should provide plans for working collaboratively with the other PCDC-RUs and the PCDC-MDCU to facilitate the discovery, clinical validation, and clinical application of biomarkers through participation in multi-institutional studies. Applicants should describe their expertise in data quality control, analysis, and interpretation of results for validation studies if they have previously participated in validation studies.

- Applicants should indicate their ability to collect pre-diagnostic and diagnostic (early stage) images (preferred, but not required), and be willing to share those for data mining and AI-based projects being developed under the sponsorship of EDNR.
- Applicants should describe any plans to provide additional archived specimens to other PCDC-RUs for discovery and/or validation studies, if they have the capability.
- Applicants should mention capabilities for prospective collection of pre-diagnostic images and/or the development of AI-based tools/methods, including working with APaCC
- Applicants should mention if they will be leveraging other consortia and resources (e.g., EDNR; Cancer of the Pancreas Screening [CAPS] Consortium; Gastrointestinal Specialized Program of Research Excellence [GI SPORE] Program; Prostate, Lung, Colorectal, and Ovarian [PLCO] Cancer Screening Trial; HMO Cancer Research Network such as Kaiser Permanente Northern California [KPNC] and Kaiser Permanente Southern California [KPSC]), international collaborations, patient advocacy groups, foundations, and have the capacity to build interconnectivity with stakeholders.
- Applicants should note that prospectively collected specimens can be used for studies proposed in their individual applications, but can also be used for collaborative activities, such as (1) sharing with other PCDC members for validation project(s), and (2) obliging with requests from non-PCDC investigators that are evaluated and recommended by the Steering Committee and approved by the NCI.

Sub-section F: Annual Milestones

The following major benchmarks of progress must be addressed. Any application lacking milestones will be considered incomplete.

Applicants should provide a clear set of annual, quantitative benchmarks for each specific aim of the PCDC-RU associated with timelines.

These milestones must be well described, quantitative, and scientifically justified. Discuss the milestones as a means for judging the success of the proposed studies. Specific aims may not be regarded as milestones (unless they include quantitative endpoints). The specific aims describe the goals and intended path of the proposed research. Quantitative milestones are a way of determining whether an applicant has successfully reached the specified goals. Applicants are expected to provide milestones for each specific aim. Milestones should be clearly stated and presented in a quantitative manner, such as numerical specifications of sensitivity and specificity, or a count of some newly discovered molecules or molecular pattern(s) that can be used as biomarkers for early detection of PDAC or risk assessment of its lethal precursors.

Examples of quantitative milestones are:

- Winnow down the search for identifying the top 10 most specific markers (DNAs, mRNAs, non-coding RNAs, metabolites, etc.) associated with early-stage pancreatic cancer;
- Phase 2 pre-validation of proteins "x, y, and z" as promising biomarkers to detect early-stage PDAC in the blood (plasma or serum);
- New molecular imaging probe tested in a pilot study in humans;
- Collection of "x" number of biospecimens per year.

Letters of Support: In addition to standard items, applicants must provide letters from the respective leadership official(s) in the institution(s) documenting specific institutional commitments for the PCDC-RU. Letters should also be included that reflect any additional resources and partnerships (e.g., for-profit sector, industry, large cohorts) that will be employed to achieve the goals of the PCDC-RU. Please also provide letters from collaborators documenting access to appropriate samples.

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the [How to Apply - Application Guide](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) (https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400).

Other Plan(s):

All instructions in the [How to Apply - Application Guide](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) (https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed, with the following additional instructions:

- A Data Management and Sharing Plan (DMS Plan) is required for any NIH-funded or conducted research that will generate scientific data. Applicants must submit the DMS Plan at the time of application using the [NIH DMS Plan Format Page](https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page) (<https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page>). The DMS Plan must address the elements in the structured format. Where the DMS Plan Format Page requires a "Yes or No" response, no additional narrative is allowed.

Appendix: Only limited Appendix materials are allowed. Follow all instructions for the Appendix as described in the [How to Apply - Application Guide](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) (https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400).

- No publications or other material, with the exception of blank questionnaires or blank surveys, may be included in the Appendix.

PHS Human Subjects and Clinical Trials Information

When involving human subjects research, clinical research, and/or NIH-defined clinical trials (and when applicable, clinical trials research experience) follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400), with the following additional instructions:

If you answered "Yes" to the question "Are Human Subjects Involved?" on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or **Delayed Onset Study** record.

Study Record: PHS Human Subjects and Clinical Trials Information

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed.

Delayed Onset Study

Note: [Delayed onset \(https://grants.nih.gov/grants/glossary.htm#DelayedOnsetStudy\)](https://grants.nih.gov/grants/glossary.htm#DelayedOnsetStudy) does NOT apply to a study that can be described but will not start immediately (i.e., delayed start). All instructions in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed.

PHS Assignment Request Form

All instructions in the [How to Apply- Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400) must be followed.

3. Unique Entity Identifier and System for Award Management (SAM)

See Part 2. Section III.1 for information regarding the requirement for obtaining a unique entity identifier and for completing and maintaining active registrations in System for Award Management (SAM), NATO Commercial and Government Entity (NCAGE) Code (if applicable), eRA Commons, and Grants.gov

4. Submission Dates and Times

Part I. contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date falls on a weekend or [Federal holiday \(https://grants.nih.gov/grants/guide/uri_redirect.html?id=82380\)](https://grants.nih.gov/grants/guide/uri_redirect.html?id=82380), the application deadline is automatically extended to the next business day.

Organizations must submit applications to [Grants.gov \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11128\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11128) (the online portal to find and apply for grants across all Federal agencies). Applicants must then complete the submission process by tracking the status of the application in the [eRA Commons \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11123\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11123), NIH's electronic system for grants administration. NIH and Grants.gov systems check the application against many of the application instructions upon submission. Errors must be corrected and a changed/corrected application must be submitted to Grants.gov on or before the application due date and time. If a Changed/Corrected application is submitted after the deadline, the application will be considered late. Applications that miss the due date and time are subjected to the [NIH Grants Policy Statement Section 2.3.9.2 Electronically Submitted Applications \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82423\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82423).

Applicants are responsible for viewing their application before the due date in the eRA Commons to ensure accurate and successful submission.

Information on the submission process and a definition of on-time submission are provided in the [How to Apply-Application Guide \(https://grants.nih.gov/grants-process/write-application/how-to-apply-application-guide\)](https://grants.nih.gov/grants-process/write-application/how-to-apply-application-guide).

5. Intergovernmental Review (E.O. 12372)

This initiative is not subject to [intergovernmental review. \(https://grants.nih.gov/grants/policy/nihgps/html5/section_10/10.10.1_executive_orders.htm\)](https://grants.nih.gov/grants/policy/nihgps/html5/section_10/10.10.1_executive_orders.htm)

6. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11120).

Pre-award costs are allowable only as described in the [NIH Grants Policy Statement Section 7.9.1 Selected Items of Cost. \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11143\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11143)

7. Other Submission Requirements and Information

Applications must be submitted electronically following the instructions described in the [How to Apply – Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400). Paper applications will not be accepted.

Applicants must complete all required registrations before the application due date. Section III. Eligibility Information contains information about registration.

For assistance with your electronic application or for more information on the electronic submission process, visit [How to Apply – Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400). If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the [Dealing with System Issues \(https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/dealing-with-system-issues.htm\)](https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/dealing-with-system-issues.htm) guidance. For assistance with application submission, contact the Application Submission Contacts in Section VII.

Important reminders:

All PD(s)/PI(s) must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile form. Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to NIH. See Section III of this NOFO for information on registration requirements.

The applicant organization must ensure that the unique entity identifier provided on the application is the same identifier used in the organization's profile in the eRA Commons and for the System for Award Management. Additional information may be found in the [How to Apply – Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400).

See [more tips \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11146\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11146) for avoiding common errors.

Upon receipt, applications will be evaluated for completeness and compliance with application instructions by the Center for Scientific Review, NIH. Applications that are incomplete or non-compliant will not be reviewed.

Mandatory Disclosure

Recipients or subrecipients must submit any information related to violations of federal criminal law involving fraud, bribery, or gratuity violations potentially affecting the federal award. See Mandatory Disclosures, [2 CFR 200.113 \(https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200/subpart-B/section-200.113\)](https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200/subpart-B/section-200.113) and [NIH Grants Policy Statement Section 4.1.35 \(https://grants.nih.gov/grants/policy/nihgps/html5/section_4/4.1.35_mandatory_disclosures.htm\)](https://grants.nih.gov/grants/policy/nihgps/html5/section_4/4.1.35_mandatory_disclosures.htm).

Send written disclosures to the NIH Chief Grants Management Officer listed on the Notice of Award for the IC that funded the award and to the [HHS Office of Inspector Grant Self Disclosure Program \(https://oig.hhs.gov/compliance/self-disclosure-info/hhs-oig-grant-self-disclosure-program/\)](https://oig.hhs.gov/compliance/self-disclosure-info/hhs-oig-grant-self-disclosure-program/) at grantdisclosures@oig.hhs.gov (<mailto:grantdisclosures@oig.hhs.gov>).

Post Submission Materials

Applicants are required to follow the instructions for post-submission materials, as described in [the policy \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82299\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82299)

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process. Applications submitted to the NIH in support of the [NIH mission](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11149) (http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11149) are evaluated for scientific and technical merit through the NIH peer review system.

Overall Impact

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following scored review criteria and additional review criteria (as applicable for the project proposed). An application does not need to be strong in all categories to be judged likely to have a major scientific impact.

Scored Review Criteria

Reviewers will consider Factors 1, 2 and 3 in the determination of scientific merit, and in providing an overall impact score. In addition, Factors 1 and 2 will each receive a separate factor score.

Factor 1. Importance of the Research (Significance and Innovation)

Significance

- Evaluate the importance of the proposed research in the context of current scientific challenges and opportunities, either for advancing knowledge within the field, or more broadly. Assess whether the application addresses an important gap in knowledge in the field, would solve a critical problem, or create a valuable conceptual or technical advance.
- Evaluate the rationale for undertaking the study, the rigor of the scientific background for the work (e.g., prior literature and/or preliminary data) and whether the scientific background justifies the proposed study.

Innovation

- Evaluate the extent to which innovation influences the importance of undertaking the proposed research. Note that while technical or conceptual innovation can influence the importance of the proposed research, a project that is not applying novel concepts or approaches may be of critical importance for the field.
- Evaluate whether the proposed work applies novel concepts, methods or technologies or uses existing concepts, methods, technologies in novel ways, to enhance the overall impact of the project.

Factor 2. Rigor and Feasibility (Approach)

Approach

- Evaluate the scientific quality of the proposed work. Evaluate the likelihood that compelling, reproducible findings will result (rigor) and assess whether the proposed studies can be done well and within the timeframes proposed (feasibility).

Rigor:

- Evaluate the potential to produce unbiased, reproducible, robust data.
- Evaluate the rigor of experimental design and whether appropriate controls are in place.
- Evaluate whether the sample size is sufficient and well-justified.
- Assess the quality of the plans for analysis, interpretation, and reporting of results.
- Evaluate whether the investigators presented adequate plans to address relevant biological variables, such as sex or age, in the design, analysis, and reporting.
- For applications involving human subjects or vertebrate animals, also evaluate:
 - the rigor of the intervention or study manipulation (if applicable to the study design).
 - whether outcome variables are justified.
 - whether the results will be generalizable or, in the case of a rare disease/special group, relevant to the particular subgroup.
 - whether the study population appropriately models the target population.
- For applications involving human subjects, including clinical trials, assess the adequacy of inclusion plans as appropriate for the scientific goals of the research. Considerations of appropriateness may include disease/condition/behavior incidence, prevalence, or population burden, population representation, and/or current state of the science.

Feasibility:

- Evaluate whether the proposed approach is sound and achievable, including plans to address problems or new challenges that emerge in the work. For proposed studies in which feasibility may be less certain, evaluate whether the uncertainty is balanced by the potential for major advances.
- For applications involving human subjects, including clinical trials, evaluate the adequacy and feasibility of the plan to recruit and retain a study population that appropriately models the target population. Additionally, evaluate the likelihood of successfully achieving the proposed enrollment based on age, race, ethnicity, and sex.
- For clinical trial applications, evaluate whether the study timeline and milestones are feasible.

Specific to this NOFO:

- Evaluate if the milestones are adequately described and will help achieve the overall goals of the PCDC.

Factor 3. Expertise and Resources (Investigator(s) and Environment)

Investigator(s)

Evaluate whether the investigator(s) have demonstrated background, training, and expertise, as appropriate for their career stage, to conduct the proposed work. For Multiple Principal Investigator (MPI) applications, assess the quality of the leadership plan to facilitate coordination and collaboration.

Environment

Evaluate whether the institutional resources are appropriate to ensure the successful execution of the proposed work.

Specific to this NOFO:

- Evaluate if the infrastructure for data storage, data security and data analysis is appropriate to support the PCDC collaborative activities (e.g., for the PCDC Prospective Cohorts).

Additional Review Criteria

As applicable for the project proposed, reviewers will consider the following additional items while determining scientific and technical merit, but will not give criterion scores for these items, and should consider them in providing an overall impact score.

Protections for Human Subjects

For research that involves human subjects but does not involve one of the categories of research that are exempt under 45 CFR Part 46, evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects; 2) adequacy of protection against risks; 3) potential benefits to the subjects and others; 4) importance of the knowledge to be gained; and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the categories of research that are exempt under 45 CFR Part 46, evaluate: 1) the justification for the exemption; 2) human subjects involvement and characteristics; and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the [Guidelines for the Review of Human Subjects \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=11175\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=11175).

Vertebrate Animals

When the proposed research includes Vertebrate Animals, evaluate the involvement of live vertebrate animals according to the following criteria: (1) description of proposed procedures involving animals, including species, strains, ages, sex, and total number to be used; (2) justifications for the use of animals versus alternative models and for the appropriateness of the species proposed; (3) interventions to minimize discomfort, distress, pain and injury; and (4) justification for euthanasia method if NOT consistent with the AVMA Guidelines for the Euthanasia of Animals. For additional information on review of the Vertebrate Animals section, please refer to the [Worksheet for Review of the Vertebrate Animals Section \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11150\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11150).

Biohazards

When the proposed research includes Biohazards, evaluate whether specific materials or procedures that will be used are significantly hazardous to research personnel and/or the environment, and whether adequate protection is proposed.

Resubmissions

As applicable, evaluate the full application as now presented.

Renewals

As applicable, evaluate the progress made in the last funding period.

Revisions

As applicable, evaluate the appropriateness of the proposed expansion of the scope of the project.

Additional Review Considerations

As applicable for the project proposed, reviewers will consider each of the following items, but will not give scores for these items, and should not consider them in providing an overall impact score.

Authentication of Key Biological and/or Chemical Resources

For projects involving key biological and/or chemical resources, evaluate the brief plans proposed for identifying and ensuring the validity of those resources.

Budget and Period of Support

Evaluate whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

2. Review and Selection Process

Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s) convened by the Center for Scientific Review (CSR), in accordance with [NIH peer review policy and procedures \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11154\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11154), using the stated review criteria. Assignment to a Scientific Review Group will be shown in the eRA Commons.

As part of the scientific peer review, all applications will receive a written critique.

Applications may undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score.

Applications will be assigned on the basis of established PHS referral guidelines to the appropriate NIH Institute or Center. Applications will compete for available funds with all other recommended applications. Following initial peer review, recommended applications will receive a second level of review by the appropriate national Advisory Council or Board. The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.
- Relevance of the proposed project to program priorities.

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant as described in the [NIH Grants Policy Statement Section 2.5.1, Just-in-Time Procedures \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=82418\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82418). This request is not a Notice of Award nor should it be construed to be an indicator of possible funding.

Prior to making an award, NIH reviews an applicant's federal award history in SAM.gov to ensure sound business practices. An applicant can review and comment on any information in the Responsibility/Qualification records available in SAM.gov. NIH will consider any comments by the applicant in the Responsibility/Qualification records in SAM.gov to ascertain the applicant's integrity, business ethics, and performance record of managing Federal awards per 2 CFR Part 200.206 "Federal awarding agency review of risk posed by applicants." This provision will apply to all NIH grants and cooperative agreements except fellowships.

3. Anticipated Announcement and Award Dates

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) via the [eRA Commons \(http://grants.nih.gov/grants/guide/redirect.htm?id=11123\)](http://grants.nih.gov/grants/guide/redirect.htm?id=11123). Refer to Part 1 for dates for peer review, advisory council review, and earliest start date.

Information regarding the disposition of applications is available in the [NIH Grants Policy Statement Section 2.4.4 Disposition of Applications \(http://grants.nih.gov/grants/guide/redirect.htm?id=82416\)](http://grants.nih.gov/grants/guide/redirect.htm?id=82416).

Section VI. Award Administration Information

1. Award Notices

A Notice of Award (NoA) is the official authorizing document notifying the applicant that an award has been made and that funds may be requested from the designated HHS payment system or office. The NoA is signed by the Grants Management Officer and emailed to the recipient's business official.

In accepting the award, the recipient agrees that any activities under the award are subject to all provisions currently in effect or implemented during the period of the award, other Department regulations and policies in effect at the time of the award, and applicable statutory provisions.

Recipients must comply with any funding restrictions described in Section IV.6. Funding Restrictions. Any pre-award costs incurred before receipt of the NoA are at the applicant's own risk. For more information on the Notice of Award, please refer to the [NIH Grants Policy Statement Section 5. The Notice of Award \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_5/5_the_notice_of_award.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_5/5_the_notice_of_award.htm) and NIH Grants & Funding website, see [Award Process. \(https://grants.nih.gov/grants/pre-award-process.htm#award\)](https://grants.nih.gov/grants/pre-award-process.htm#award)

Individual awards are based on the application submitted to, and as approved by, the NIH and are subject to the IC-specific terms and conditions identified in the NoA.

ClinicalTrials.gov: If an award provides for one or more clinical trials. By law (Title VIII, Section 801 of Public Law 110-85), the "responsible party" must register and submit results information for certain "applicable clinical trials" on the ClinicalTrials.gov Protocol Registration and Results System Information Website (<https://register.clinicaltrials.gov> (<https://register.clinicaltrials.gov/>)). NIH expects registration and results reporting of all trials whether required under the law or not. For more information, see <https://grants.nih.gov/policy/clinical-trials/reporting/index.htm> (<https://grants.nih.gov/policy/clinical-trials/reporting/index.htm>).

Institutional Review Board or Independent Ethics Committee Approval: Recipient institutions must ensure that all protocols are reviewed by their IRB or IEC. To help ensure the safety of participants enrolled in NIH-funded studies, the recipient must provide NIH copies of documents related to all major changes in the status of ongoing protocols.

Data and Safety Monitoring Requirements: The NIH policy for data and safety monitoring requires oversight and monitoring of all NIH-conducted or -supported human biomedical and behavioral intervention studies (clinical trials) to ensure the safety of participants and the validity and integrity of the data. Further information concerning these requirements is found at http://grants.nih.gov/grants/policy/hs/data_safety.htm (http://grants.nih.gov/grants/policy/hs/data_safety.htm) and in the application instructions (SF424 (R&R) and PHS 398).

Investigational New Drug or Investigational Device Exemption Requirements: Consistent with federal regulations, clinical research projects involving the use of investigational therapeutics, vaccines, or other medical interventions (including licensed products and devices for a purpose other than that for which they were licensed) in humans under a research protocol must be performed under a Food and Drug Administration (FDA) investigational new drug (IND) or investigational device exemption (IDE).

2. Administrative and National Policy Requirements

The following Federal wide and HHS-specific policy requirements apply to awards funded through NIH:

- The rules listed at [2 CFR Part 200 \(https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200\)](https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200), Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards.
- All NIH grant and cooperative agreement awards include the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/redirect.htm?id=11120) as part of the terms and conditions in the Notice of Award (NoA). The NoA includes the requirements of this NOFO. For these terms of award, see the [NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General \(http://grants.nih.gov/grants/guide/redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/redirect.htm?id=11120) and [Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Recipients, and Activities \(http://grants.nih.gov/grants/guide/redirect.htm?id=11159\)](http://grants.nih.gov/grants/guide/redirect.htm?id=11159).

All federal statutes and regulations relevant to federal financial assistance, including those highlighted in [NIH Grants Policy Statement Section 4 Public Policy Requirements, Objectives and Other Appropriation Mandates. \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_4/4_public_policy_requirements_objectives_and_other_appropriation_mandates.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_4/4_public_policy_requirements_objectives_and_other_appropriation_mandates.htm)

By applying for or accepting federal funds from HHS, recipients certify compliance with all federal antidiscrimination laws and these requirements and that complying with those laws is a material condition of receiving federal funding streams. Recipients are responsible for ensuring subrecipients, contractors, and partners also comply.

Applicants and recipients are strongly encouraged to refer to the [NIH Director's Statement of Priorities \(https://www.nih.gov/about-nih/nih-director/statements/advancing-nih-mission-through-unified-strategy\)](https://www.nih.gov/about-nih/nih-director/statements/advancing-nih-mission-through-unified-strategy), entitled "Advancing NIH's Mission Through a Unified Strategy."

Recipients are responsible for ensuring that their activities comply with all applicable federal regulations. Pursuant to 2 CFR 200.340, by accepting an NIH award, the recipient agrees that continued funding for the award is contingent upon the availability of appropriated funds, recipient satisfactory performance, compliance with the Terms and Conditions of the award, and may also otherwise be terminated, to the extent authorized by law, if the agency determines that the award no longer effectuates the program goals or agency priorities, in line with 2 CFR 200.340(a)(4).

Pursuant to the Cybersecurity Act of 2015, Div. N, § 405, Pub. Law 114-113, 6 USC § 1533(d), the HHS Secretary has established a common set of voluntary, consensus-based, and industry-led guidelines, best practices, methodologies, procedures, and processes.

Successful recipients under this NOFO agree that:

When recipients, subrecipients, or third-party entities have:

- ongoing and consistent access to HHS owned or operated information or operational technology systems; and
- receive, maintain, transmit, store, access, exchange, process, or utilize personal identifiable information (PII) or personal health information (PHI) obtained from the awarding HHS agency for the purposes of executing the award.

Cybersecurity plans and procedures **must** at minimum include the following:

- Develop cybersecurity plans and procedures, modeled after the [NIST Cybersecurity framework \(https://www.nist.gov/cyberframework\)](https://www.nist.gov/cyberframework), to protect HHS systems and data:
 - Identify:**
 - Develop an inventory of all assets and accounts with access to HHS owned and operated information or operational technology systems or which obtain PII or PHI for the purposes of the award.
 - Protect:**
 - Limit access to HHS owned and operated systems to only those in need of access to complete reward activities.
 - Require all staff to complete annual cybersecurity and privacy awareness training. Visit [405\(d\): Knowledge on Demand \(hhs.gov\) \(https://405d.hhs.gov/kod/five-threats\)](https://405d.hhs.gov/kod/five-threats) to obtain free trainings, if needed.

- Enable multifactor authentication for all employees, subrecipients, and third-party entities to access HHS owned and operated information or operational technology systems.
- Regularly backup sensitive data and test backups.
- **Detect:**
 - Install anti-virus or anti-malware software on all devices, servers, and accounts used to connect to HHS owned and operated systems.
- **Respond:**
 - Develop an incident response plan. See [Incident-Response-Plan-Basics_508c.pdf \(cisa.gov\)](https://www.cisa.gov/sites/default/files/publications/Incident-Response-Plan-Basics_508c.pdf) (https://www.cisa.gov/sites/default/files/publications/Incident-Response-Plan-Basics_508c.pdf) to learn about developing incident response plans.
 - Have cybersecurity incident reporting procedures that ensure the relevant HHS awarding agencies are notified of a cybersecurity incident within 48 hours of discovery. A cybersecurity incident is defined as an unplanned interruption to a technology service or reduction in the quality of a technology service, or an occurrence that actually or potentially jeopardizes the confidentiality, integrity, or availability of an information system or the information the system processes, stores, or transmits.
- **Recover:**
 - Investigate incidents and plug any security gaps identified.

All activities proposed in your application and budget narrative must align with applicable law, including but not limited to statutes, executive orders, federal regulations and applicable judicial holdings. Accordingly, discretionary awards shall not be used to fund, promote, encourage, subsidize, or facilitate; racial preferences or other forms of racial discrimination by the recipient, including activities where race or intentional proxies for race will be used as a selection criterion for employment or program participation; denial by the recipient of the sex binary in humans, or the belief that sex is a chosen or mutable characteristic; illegal immigration; or any other initiatives that compromise public safety. If an application does not align, the application will not receive funding to the extent permitted by law and applicable court orders.

For applications involving substance abuse, the application must not support harm reduction. Please see [Updated Funding Guidance for Recipients on Supplies and Services](https://www.samhsa.gov/sites/default/files/dear-colleague-letter-updated-hr-funding-guidance.pdf) (<https://www.samhsa.gov/sites/default/files/dear-colleague-letter-updated-hr-funding-guidance.pdf>).

For applications involving funding Medication-Assisted Treatment (MAT) or medications for opioid use disorder (MOUD), this funding should be used to provide comprehensive treatment and recovery support services rather than medication-only models for opioid use disorder. Services should include medications, where clinically indicated, in conjunction with psychosocial and other treatment and recovery support services. Funding can also be used to support individualized tapering and discontinuation of medications when clinically indicated. Please see [Updated Funding Guidance for Recipients on MAT/MOUD](https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.samhsa.gov%2Fsites%2Fdefault%2Ffiles%2Fdear-colleague-letter-mat-moud-guidance.pdf&data=05%7C02%7Cchelsey.hughes%40nih.gov%7C725bb62d1f94a2b9ff908dec0bc5a25%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C63916011238415) (<https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.samhsa.gov%2Fsites%2Fdefault%2Ffiles%2Fdear-colleague-letter-mat-moud-guidance.pdf&data=05%7C02%7Cchelsey.hughes%40nih.gov%7C725bb62d1f94a2b9ff908dec0bc5a25%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C63916011238415>).

As of October 1, 2025, HHS has adopted [2 CFR Part 200](https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200) (<https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200>), with some modifications included in 2 CFR Part 300. These regulations replace those in 45 CFR Part 75. However, for NIH, under the Consolidated Appropriations Act for FY 2026, ([P.L. 119-75](https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.congress.gov%2Fbills%2F119th-congress%2Fhouse-bill%2F7148&data=05%7C02%7Cantoine.caliman%40nih.gov%7C68a8e1e3db804c61b38f08deb0e88127%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C63914270982)) (<https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.congress.gov%2Fbills%2F119th-congress%2Fhouse-bill%2F7148&data=05%7C02%7Cantoine.caliman%40nih.gov%7C68a8e1e3db804c61b38f08deb0e88127%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C63914270982>), the provisions relating to indirect costs in 45 CFR 75 continue to apply to NIH awards. Consistent with the statute, NIH will not apply updated thresholds outlined within 2 CFR Part 200, at this time.

In administering programs under this and all funding announcements, NIH prioritizes:

- Research involving rigorous scientific methods, including for studies related to children and adolescents, where NIH is committed to approaches that reflect the highest standards of clinical care and child safety.
- Biological and physiological integrity: Recognizing the relevance of biological sex to health outcomes, NIH encourages applicants to account for sex-based health factors in program design, data collection, and service delivery where scientifically appropriate.
- NIH will implement these priorities consistent with applicable laws, regulations, court orders, and all required administrative procedures. Applicants are encouraged to describe how their proposed programs align with these priorities in their project narratives. Funded activities must advance NIH's vision of protecting and improving the health and well-being of Americans. The particular focus is on those who are medically vulnerable, or live in areas with limited access to care. NIH's duty is to serve wisely, effectively, and with measurable results that justify every taxpayer dollar invested.

Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (HHS) grant administration regulations at 2 CFR Part 200, 45 CFR 75 (for indirect cost provisions), and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the recipients is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the recipients for the project as a whole, although specific tasks and activities may be shared among the recipients and NIH as defined below.

The PD(s)/PI(s) will have the primary responsibility for:

- Defining the scientific objectives and approaches and overseeing the scientific research in the RU, including research design and study protocol development, participant recruitment and follow-up (if applicable), data collection, quality control, interim data and safety monitoring, analyzing and interpreting research data, reporting results to the scientific community and publishing results. Actively participating in the PCDC, including collaboration, meetings, and scientific workshops; attending two annual Steering Committee meetings (one in-person, one virtual).
- Serving on the PCDC Steering Committee and participating as a voting member of the Steering Committee.
- Organizing scientific working groups to facilitate collaborative projects and cross-testing of experimental, analytical and validation concepts.
- Abiding by the governance of the PCDC.
- Coordinating the RU efforts within PCDC and cooperating with the other research units of the Network and with NCI staff members.
- Sharing data, materials, and resources, and disseminating tools and outputs to the broader scientific community.
- Reporting progress including obstacles and challenges, to the NCI Program Officials.
- Participating in NCI-led program evaluations, including required reports and a site visit during the project period.
- Coordinate the transfer of biospecimens to the NCI at Frederick Central Repository.
- Recipients will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies.

PDs/PIs Responsibilities for Network Collaborative Studies:

- Accepting and implementing the goals, priorities, common study protocols, procedures, and policies agreed upon by the Steering Committee for the individual and Network collaborative studies to the extent consistent with grant regulations.

- Ensuring Network and NCI review and approval of study protocols, concepts, final protocol documents, informed consents, and study amendments, and advising/informing NCI of changes in study protocol status.
- Collaborating on common study designs or protocols, including methods and requirements for joint participation and collaboration as recommended by the Steering Committee, and handling of data, including appropriate sharing of methods and data among collaborating organizations.
- Accruing subjects on collaborative studies approved by the Steering Committee. Awardees will be expected to submit information on specimen collections per PCDC-developed CDEs and register their study protocols with the MDCU.
- Participating in the collection of samples for the Prospective Cohorts and Reference Sets is required.

NIH staff have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

A designated NCI Program Official serving as the Project Coordinator will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below. Additional NCI staff members may also become substantially involved as needed. An NCI Program Director acting as Program Official will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice. Additional Program Officials who are not responsible for the normal scientific and programmatic stewardship of the award may be designated as Project Scientists and assist in Network activities.

The specific roles of the substantially involved NCI Program Officer include the following activities:

- Coordinating and facilitating various activities of the PCDC program.
- Participating in the activities of the PCDC Steering Committee as voting and/or non-voting members.
- Serving as a liaison between the Steering Committee, the PCDC awardees, and the NIH;
- Ensuring that there is effective communication across the Network.
- Assisting the Steering Committee in developing and drafting Network operating policies.
- Facilitating collaborative research efforts that involve multiple PCDC awardees.
- Assist recipients in leveraging NIH/NCI resources, such as the Frederick Central Repository, and disseminating outputs.
- Co-organize and participate in PCDC meetings.
- Monitor scientific progress and compliance with Steering Committee recommendations.
- Establish working groups and cross-PCDC projects as needed.
- Approve use of set-aside funds for Steering Committee-endorsed activities.
- Assist recipients in leveraging NIH/NCI resources and disseminating outputs.

Areas of Joint Responsibility include:

Steering Committee: The Steering Committee will be the main governing body for the PCDC. The PCDC Steering Committee will convene after all the Network units have been funded and will be composed of the following voting members:

- All PDs/PIs representing each PCDC U01/U24 award.
- The NCI-designated Project Coordinator.

Each voting member will have one vote. The NCI Project Coordinator will have one vote on behalf of all NIH participants.

NIH staff and other experts may participate as non-voting members, as needed.

The Steering Committee Chair (non-NIH) is selected by the Committee.

The Committee meets twice annually (one in-person, one virtual).

Working groups may be established, with participation from NCI staff as appropriate.

Primary responsibilities of the Steering Committee include, but are not limited to, the following activities:

- Identify consortium-level scientific and policy issues and recommend actions to NCI.
- Update and refine policies for collaborative projects, protocols, and underperforming studies; recommend replacement projects within existing budgets.
- Review patient accrual, compliance, audits, and regulatory requirements; report findings to NCI.
- Oversee the PCDC Manual of Operations, biorepository efforts, and guidelines for specimen sets and Signature Cohorts.
- Set research priorities, identify emerging opportunities, and promote trans-PCDC initiatives.
- Track research progress and ensure timely publication of results.
- Review and prioritize collaborative projects, oversee data submission and access policies, and advise NCI on use of set-aside funds.
- Evaluate validation data to determine readiness or discontinuation of assays.
- Monitor overall consortium performance and promote use of NIH/NCI resources.
- Ensure compliance with resource sharing and intellectual property policies across all collaborators.
- Support outreach to the broader research community.
- Identifying scientific and policy issues that need to be, or can benefit by being, addressed at the

Dispute Resolution:

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between recipients and NIH may be brought to Dispute Resolution. A Dispute Resolution Panel composed of three members will be convened: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual recipient. This special dispute resolution procedure does not alter the recipient's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D and HHS regulation 45 CFR Part 16.

3. Data Management and Sharing

A Data Management and Sharing Plan (DMS Plan) is required for any NIH-funded or conducted research that will generate scientific data. Applicants must submit the DMS Plan at the time of application using the [NIH DMS Plan Format Page \(https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page\)](https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page). The DMS Plan must address the elements in the structured format. Where the DMS Plan Format Page requires a "Yes or No" response, no additional narrative is allowed.

4. Reporting

When multiple years are involved, recipients will be required to submit the [Research Performance Progress Report \(RPPR\) \(http://grants.nih.gov/grants/rppr/index.htm\)](http://grants.nih.gov/grants/rppr/index.htm) annually and financial statements as required in the [NIH Grants Policy Statement Section 8.4.1 Reporting. \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_8/8.4.1_reporting.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_8/8.4.1_reporting.htm) To learn more about post-award monitoring and reporting, see the NIH Grants & Funding website, see [Post-Award Monitoring and Reporting \(https://grants.nih.gov/grants/guide/url_redirect.php?id=82428\)](https://grants.nih.gov/grants/guide/url_redirect.php?id=82428).

A final RPPR, invention statement, and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as described in the [NIH Grants Policy Statement Section 8.6 Closeout \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=82420\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82420). NIH NOFOs outline intended research goals and objectives. Post award, NIH will review

and measure performance based on the details and outcomes that are shared within the RPPR, as described at 2 CFR Part 200.301.

Section VII. Agency Contacts

We encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants. When contacting the email addresses below please add the NOFO number to the subject line to assist routing.

Application Submission Contacts

[eRA Service Desk \(https://www.era.nih.gov/need-help\)](https://www.era.nih.gov/need-help) - Questions regarding ASSIST, eRA Commons, application errors and warnings, documenting system problems that threaten submission by the due date, and post-submission issues.

[Grants.gov Support Center \(https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fgrants.gov%2Fsupport&data=05%7C02%7Cantoinette.caliman%40nih.gov%7Caf6dde64d644478d4e8b08dde6700581%7C14b77578977342d58507251ca2dc2b](https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fgrants.gov%2Fsupport&data=05%7C02%7Cantoinette.caliman%40nih.gov%7Caf6dde64d644478d4e8b08dde6700581%7C14b77578977342d58507251ca2dc2b)

- Questions regarding Grants.gov registration and services (e.g., Workspace, subscriptions).

Scientific/Research Contact(s)

Cancer Biomarker Branch

National Cancer Institute (NCI)

Email: ncipcdc@nih.gov (<mailto:ncipcdc@nih.gov>)

Peer Review Contact(s)

Examine your eRA Commons account for review assignment and contact information (information appears two weeks after the submission due date).

Financial/Grants Management Contact(s)

Office of Grants Administration

National Cancer Institute (NCI)

E-mail: NCIFinancialContact@nih.gov (<mailto:NCIFinancialContact@nih.gov>)

Section VIII. Other Information

Recently issued trans-NIH [policy notices \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11163\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11163) may affect your application submission. A full list of policy notices published by NIH is provided in the [NIH Guide for Grants and Contracts \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164). All awards are subject to the terms and conditions, cost principles, and other considerations described in the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Authority and Regulations

Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR Part 52 and 2 CFR Part 200.