Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)

National Institutes of Health (NIH (http://www.nih.gov))

Components of Participating Organizations

National Cancer Institute (NCI (http://grants.nih.gov/grants/guide/url_redirect.htm?id=82468))

National Institute of Environmental Health Sciences (NIEHS (http://grants.nih.gov/grants/guide/url_redirect.htm?id=82482))

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). ICOs that do not participate in this announcement will not consider applications for funding.

Funding Opportunity Title

Early-Onset Cancers: Investigating Etiology, Mechanisms, and Early Detection Strategies (RP1 Clinical Trials Optional)

Activity Code

RP1 (https://grants.nih.gov/funding/activity-codes/RP1) Science-Driven Research Project

Announcement Type

New

Related Notices

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

Funding Opportunity Number (FON)

PAR-28-014

Companion Funding Opportunity

None

Number of Applications

See Part 2, Section III. 3. Additional Information on Eligibility.

Assistance Listing Number(s)

93.393, 93.113

Funding Opportunity Purpose

This Notice of Funding Opportunity (NOFO) invites applications that investigate the etiology of sporadic non-hereditary early-onset cancers (EOCs: ages 18 to 49 years) and the underlying biological mechanisms that play a role in these cancers to inform prevention and control strategies. The proposed research is expected to advance the understanding of the unexplained rise of cancers in young adults. More specifically, studies should focus on one or more of the following: i) identifying what environmental or lifestyle exposures are driving the increase in the incidence of non-hereditary EOCs, and how these factors vary by patient demographics; ii) examining the biological mechanisms and host responses that underlie the increase in EOCs; and iii) identifying how those at increased risk of developing EOCs can be identified more effectively.

In an effort to streamline the application process and sustain momentum in this critical research area, this NOFO supports both exploratory/developmental and standard research projects through a grant award instrument.

Funding Opportunity Goal(s)

To identify cancer risks and risk reduction strategies, to identify how these risks cause cancer in humans, and to discover and develop mechanisms for cancer prevention and preventive interventions in humans.

Key Dates

Posted Date

October 14, 2026

Open Date (Earliest Submission Date)

January 08, 2027

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 08, 2027	February 08, 2027	Not Applicable	July 2027	October 2027	December 2027
June 08, 2027	June 08, 2027	Not Applicable	November 2027	January 2028	April 2028
October 13, 2027	October 13, 2027	Not Applicable	March 2028	May 2028	July 2028
February 08, 2028	February 08, 2028	Not Applicable	July 2028	October 2028	December 2028
June 08, 2028	June 08, 2028	Not Applicable	November 2028	January 2029	April 2029
October 11, 2028	October 11, 2028	Not Applicable	March 2029	May 2029	July 2029
February 08, 2029	February 08, 2029	Not Applicable	July 2029	October 2029	December 2029
June 08, 2029	June 08, 2029	Not Applicable	November 2029	January 2030	April 2030
October 11, 2029	October 11, 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

October 12, 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), 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)).

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.

Table of Contents

Part 1. Overview Information
- Key Dates

Part 2. Full Text of Announcement
- Section I. Notice of Funding Opportunity Description
- Section II. Award Information
- Section III. Eligibility Information
- Section IV. Application and Submission Information
- Section V. Application Review Information
- Section VI. Award Administration Information
- Section VII. Agency Contacts
- Section VIII. Other Information

Part 2. Full Text of Announcement

Section I. Notice of Funding Opportunity Description

Key Definitions for this NOFO

Early-onset Cancers (EOCs). For the purpose of this NOFO, cancers occurring in adults between the ages of 18 and 49 years (also referred to as young-onset cancers) but are distinct from pediatric and adolescent and young adult (AYA) cancers, which differ in their biological characteristics.

Background

Cancers historically diagnosed in older adults–such as colorectal, breast, uterine, kidney, and pancreatic–are now increasingly affecting younger adults. The incidence of EOCs has been rising globally since the 1990s and is projected to increase by 31% by 2030. Mortality rates from EOCs rose by 27.7% between 1990 and 2019 and are projected to increase by 21% by 2030. To date, most research has primarily focused on early-onset colorectal cancers (EOCRCs) in which increasing incidence rates among younger adults were first reported. Equally critical is the need to investigate the causes of rising incidences of other EOCs. Research is therefore needed to address the substantial knowledge gaps regarding why cancer is shifting to younger adults.

Differences in clinical presentation may provide important insight into the underlying pathogenesis of EOCs. For instance, EOCRCs typically occur in the distal colon and rectum, compared with late-onset disease where proximal tumors predominate. Pancreatic tumors in the early-onset group tend to be in the tail rather than the head as is more commonly found in those with late-onset disease. Understanding the molecular and genetic factors that control host responses to environmental drivers of EOCs is critical for characterizing risk factors and developing new biologically-based approaches for early cancer detection and intervention strategies for people younger than 50, as a lower index of suspicion of cancer in symptomatic younger individuals may compromise early detection and lead to late-stage diagnosis.

While it is unclear what is driving the increase in cancer incidence in younger adults, the data are unlikely to be explained by increased detection of rare genetic syndromes. The observed increase in cancer rates in young adults may be attributable to changes in potentially modifiable exposures in early life, adolescence, and/or young adulthood in successively younger generations. Some environmental exposures that have changed since the 1970s and have been hypothesized to play a role in EOC include diet (e.g., ultra-processed foods, sugary beverages), lifestyle factors (e.g., alcohol consumption, sleep patterns, physical inactivity, obesity), antibiotic use, and environmental pollutants (e.g., air, endocrine disrupting chemicals, microplastics, etc.). Other understudied exposures, such as social stressors and more contemporary exposures (e.g., personal care products, cannabis use) may also be responsible for the rising incidence of cancer in younger adults. In addition, the underlying biological mechanisms (e.g., gene-environment interactions, cell signaling pathways, accelerated aging) through which these exposures may contribute to EOCs are unknown.

EOC trends have also mirrored the large increase in the prevalence of overweight and obesity among young people. Evidence from animal models suggests that obesity reduces the length of latency and that tumor-promoting effects of obesity may endure after subsequent weight loss. Unlike the consistent evidence that excess body weight is associated with increased risk of late-onset cancers, its role in EOCs is unclear and the effect of excess body weight during childhood or that of weight cycling during different stages of development is not well-characterized. It will be critical to outline how these different risk factors converge to initiate EOCs.

Scope and Research Objectives of this NOFO

The goal of this NOFO is to solicit multidisciplinary studies that investigate the underlying causes and mechanisms of EOCs and develop strategies to address these factors via targeted prevention and control strategies in younger adults. Submitted applications should address one or more of the following topic areas:

(1) what environmental exposures or lifestyle factors are driving the increase in the incidence of non-hereditary EOCs, and how do these factors vary by sex, race, ethnicity, geography, or genetics?

(2) what biological mechanisms and host responses underlay the increase in EOCs?

(3) how can we more effectively identify patients at increased risk of developing EOCs?

The initiative's primary focus is on understanding the etiology and biology of sporadic EOCs. Priorities will emphasize understudied EOCs that have shown reported rising incidence trends in young adults, including early-onset uterine, pancreatic, and kidney cancers. Applications addressing other cancers, such as EOCRC and early-onset female breast cancers, will also be considered where they present compelling scientific rationale aligning with the initiative's overarching objectives. Emphasis will also be placed on studies that propose combined methodologies (e.g., epidemiologic studies and laboratory-based methods) or span from preclinical to population-based studies and propose unique scientific partnerships to address the role of understudied exposures, such as environmental pollutants or contemporary lifestyle exposures and their underlying mechanisms in EOCs. Research studies that incorporate relevant sociodemographic characteristics and/or geography are also encouraged.

Specific Areas of Research Interest

The following are examples of research areas that are within the scope of this NOFO but are not limited to those listed below.

Etiology and Mechanism:

- Identify environmental and lifestyle exposures that contribute to the etiology of EOCs;
- Characterize perturbations to normal cellular and molecular pathways of early-life influences/exposures that explain the increasing EOC incidence;
- Conduct studies that integrate innovative technologies, cancer models, and study designs to identify potential carcinogenic mechanisms and other biological signatures shared across different EOC types;
- Develop and use novel and targeted models to understand the underlying mechanisms of EOC;
- Conduct studies to assess the timing/critical window of early-life environmental exposures using preclinical models and population-based studies;
- Evaluate the role of non-intrinsic factors such as microbiota in mediating cancer risk and treatment effectiveness in individuals diagnosed with EOC;
- Determine the underlying mechanisms contributing to observed sociodemographic differences in incidence of EOCs;
- Explore the mechanistic details of novel environmental exposures and their interactions with specific genetic, epigenetic, or biological pathways, that contribute to EOCs;
- Determine if a relationship exists between accelerated aging and EOCs.

Methods to Identify Those with Increased Susceptibility for EOCs

- Develop computational and AI models to assist in risk stratification for EOC;
- Identify and characterize biomarkers associated with EOC.
- Assess environmental exposures and lifestyle factors using exposomics to assess EOC risks.

Non-responsive Applications

Applications submitted in response to this NOFO that propose any of the following will not be reviewed:

- Applications that focus on survivorship issues;
- Applications that focus only on cancers diagnosed in individuals over 50 years of age or those diagnosed under the age of 18 (i.e., pediatric population);
- Applications that focus significantly on hereditary/familial cancer syndrome (e.g., Lynch syndrome, Li-Fraumeni syndrome, etc.) or rare germline genetic variation with high penetrance;
- Applications that focus on cancers in younger adults where incidence rates are decreasing (e.g., lung, prostate, liver);
- Applications that focus on screening in the general population.

In addition to standard research projects, this NOFO supports exploratory research projects. Exploratory projects include those that are in early and conceptual stages and may involve considerable risk that has the potential to lead to a breakthrough or major development in a field of biomedical, behavioral, or clinical research.

Note to Early Stage Investigators (ESIs): Regardless of the type of application submitted (standard or exploratory), PD/PIs will not maintain their ESI status upon receipt of an RP1 award. ESIs are encouraged to apply for standard research projects when appropriate for the proposed research. ESIs will receive special consideration during the review and funding process.

Investigators proposing NIH-defined clinical trials may refer to the Research Methods Resources (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

Grant: A financial assistance mechanism providing money, property, or both to an eligible entity to carry out an approved project or activity.

Application Types Allowed

New
Resubmission
Revision

The OER Glossary (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)

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

For exploratory/developmental research projects, application budget is limited to $200,000 per year in direct costs.

For standard research projects, application budget is limited to $500,000 per year in direct costs.

Budget should reflect the actual needs of the proposed project.

Award Project Period

The maximum project period is 3 years for exploratory/developmental research projects and 5 years for standard research projects.

NIH grants policies as described in the NIH Grants Policy Statement (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
- Non-domestic (non-U.S.) Entities (Foreign Organizations)

Foreign Organizations/International Collaborations

Non-domestic (non-U.S.) Entities (Foreign Organizations) **are** eligible to apply.

Non-domestic (non-U.S.) components of U.S. Organizations **are** eligible to apply.

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

NIH will no longer issue awards (i.e., new, renewal, or non-competing continuation) to domestic or foreign entities that involve foreign subawards/subcontracts. All NIH-funded research involving foreign subawards/subcontracts must be submitted in response to a NOFO that is specifically designated for funded international collaborations. See NIH Grants Policy Statement 16.8 Collaborative International Research Awards (https://grants.nih.gov/grants/policy/nihgps/HTML5/section_16/16.8_collab_int_res_awards.htm).

Applications involving foreign subawards/subcontracts submitted in response to this NOFO will be deemed noncompliant and will not be considered for funding. This policy applies to all monetary international collaborations resulting in foreign subawards/subcontracts, however, it does not preclude unfunded international collaborations or foreign components (https://grants.nih.gov/grants/policy/nihgps/HTML5/section_1/1.2_definition_of_terms.htm), funding for foreign consultants, or procurement of unique equipment or supplies from foreign vendors.

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) for additional information.

- System for Award Management (SAM) (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) (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) - 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) – 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. Obtaining an eRA Commons account can take up to 2 weeks.

All PD(s)/PI(s) must be registered with ORCID (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).

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.

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).

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/url_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/url_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/url_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/url_redirect.php?id=11163), or other notice from NIH Guide for Grants and Contracts (https://grants.nih.gov/grants/guide/url_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.

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) and should be used for preparing an application to this NOFO.

Application Options	Project Period Limit	Page Limit
Exploratory	1-3 years	6 pages
Standard	4-5 years	12 pages

Check your application carefully prior to submission. These limits may be enforced by NIH staff, rather than through system validations.

SF424(R&R) Cover

All instructions in the How to Apply - Application Guide (https://grants.nih.gov/grants/guide/url_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-process/write-application/how-to-apply-application-guide) must be followed.

SF424(R&R) Other Project Information

All instructions in the How to Apply- Application Guide (https://grants.nih.gov/grants-process/write-application/how-to-apply-application-guide) must be followed.

SF424(R&R) Senior/Key Person Profile

All instructions in the How to Apply- Application Guide (https://grants.nih.gov/grants-process/write-application/how-to-apply-application-guide) must be followed.

Specific to this NOFO: Describe the multidisciplinary expertise available for the project, particularly if combined methodologies are proposed, and the team's complementary scientific expertise that can facilitate the proposed research.

R&R Budget

All instructions in the How to Apply- Application Guide (https://grants.nih.gov/grants-process/write-application/how-to-apply-application-guide) must be followed.

Specific to this NOFO: The travel budget should include funds to attend the annual investigators' meeting to discuss progress on the grant projects, share knowledge, and address challenges.

R&R Subaward Budget

All instructions in the How to Apply-Application Guide (https://grants.nih.gov/grants-process/write-application/how-to-apply-application-guide) must be followed.

PHS 398 Cover Page Supplement

All instructions in the How to Apply- Application Guide (https://grants.nih.gov/grants-process/write-application/how-to-apply-application-guide) must be followed.

PHS 398 Research Plan

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

Requirements

- Although preliminary data are not required for exploratory/developmental research project applications, they may be included to support the proposed research.
- A standard research project application is required to have sufficient background material or preliminary information to justify the importance and feasibility of the proposed research whererobust experiments are designed, potential experimenter biases are minimized, results and analyses are transparently reported, and results are interpreted carefully. These recommended research practices include, where applicable, expressing clear rationale for the chosen model(s) and primary/secondary endpoint(s), describing tools and parameters clearly, blinding, randomizing, enduring adequate sample size, pre-specifying inclusion/exclusion criteria, appropriately handling missing data and outliers, implementing appropriate controls, preplanning analyses, and using appropriate quantitative techniques. It is also strongly recommended to indicate clearly the exploratory vs. confirmatory components of the study, consider study limitations, and plan for transparent reporting of all methods, analyses, and results so that other investigators can evaluate the quality of the work and potentially perform replications.
- Investigators should indicate whether data presented or cited in the application as key support for the proposed work were collected, analyzed, and reported in a rigorous and transparent manner as indicated above. A plan to address any ambiguity, weaknesses, or limitations in the prior research should be included in the application. Proposed experiments should similarly adhere to these high standards of rigor and transparency.

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-process/write-application/how-to-apply-application-guide).

Other Plan(s):

All instructions in the How to Apply-Application Guide (https://grants.nih.gov/grants-process/write-application/how-to-apply-application-guide) 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). 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-process/write-application/how-to-apply-application-guide).

- 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-process/write-application/how-to-apply-application-guide), 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-process/write-application/how-to-apply-application-guide) must be followed.

Delayed Onset Study

Note: Delayed onset (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-process/write-application/how-to-apply-application-guide)must be followed.

PHS Assignment Request Form

All instructions in the How to Apply- Application Guide (https://grants.nih.gov/grants-process/write-application/how-to-apply-application-guide) must be followed.

Foreign Organizations

Foreign (non-U.S.) organizations must follow policies described in the NIH Grants Policy Statement (http://grants.nih.gov/grants/guide/url_redirect.htm?id=11137), and procedures for foreign organizations described throughout the How to Apply- Application Guide.

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/url_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/url_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/url_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 (http://grants.nih.gov/grants/guide/url_redirect.htm?id=11128) 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/url_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).

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)

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/url_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/url_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-process/write-application/how-to-apply-application-guide). 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/url_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) 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-process/write-application/how-to-apply-application-guide).

See more tips (http://grants.nih.gov/grants/guide/url_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 and responsiveness by components of participating organizations, NIH. Applications that are incomplete, non-compliant and/or nonresponsive 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) 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).

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/) 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/url_redirect.htm?id=82299)

Any instructions provided here are in addition to the instructions in the policy.

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/url_redirect.htm?id=11149) are evaluated for scientific and technical merit through the NIH peer review system.

For this particular announcement, note the following:

Exploratory/developmental research projects support investigation of novel scientific ideas or new model systems, tools, or technologies that have the potential for significant impact on biomedical research. An exploratory/developmental research project application should not have extensive background material or preliminary information. Accordingly, reviewers will emphasize the conceptual framework, the level of innovation, and the potential to significantly advance knowledge or understanding. Appropriate justification for the proposed work can be provided through literature citations, data from other sources, or, when available, from investigator-generated data. While preliminary data is not required for exploratory/developmental applications, it may be included if available.

A standard research project application is required to have sufficient background material or preliminary information to justify the importance and feasibility of the proposed research.

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.

Specific to this NOFO

- Evaluate if the project will address important gaps in knowledge, including but not limited to novel, emerging, understudied, or combined exposures of interest and their windows of susceptibility.
- Evaluate if novel and understudied biological pathways underlying EOCs will be studied.
- Evaluate whether the application proposes to study understudied and/or rare cancer types in young adults (18 to 49 years old).
- Evaluate if the application describes how the proposed project will inform future cancer prevention and intervention strategies to decrease the EOC burden in the United States.

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 the availability of and access to appropriate models and specimen resources that can support the EOC being studied.
- Evaluate the novelty of the proposed measures of relevant exposures to EOCs and highlight the innovation of these methods.

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.

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).

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).

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.

Inclusion of Human Subjects Policies

When the proposed project involves human subjects and/or NIH-defined clinical research, the committee will evaluate the proposed plans for inclusion. For additional information on review of the Inclusion section, please refer to the Guidelines for the Review of Inclusion in Clinical Research (http://grants.nih.gov/grants/guide/url_redirect.htm?id=11174).

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 CSR, in accordance with NIH peer review policies and practices (https://grants.nih.gov/policy-and-compliance/policy-topics/peer-review), 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). 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/url_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/url_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) and NIH Grants & Funding website, see Award Process. (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), 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/url_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/url_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/url_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)

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-nihs-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), 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) 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) 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-upated-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://www.samhsa.gov/sites/default/files/dear-colleague-letter-mat-moud-guidance.pdf).

Recipients of both Clinical Trial Required and Clinical Trial Optional awards subject to this term shall report standardized clinical trial activation and enrollment performance data for any interventional (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-26-063.html)clinical trial supported under the award. These metrics are intended to assess trial startup efficiency, site activation, and post-activation performance and to support continuous quality improvement in clinical trial operations (see supplemental guidance). Recipients shall report required data annually at the time of Research Performance Progress Report (RPPR) submission on clinical trial activation and enrollment performance milestone dates as calendar dates; NIH will calculate standardized interval metrics from these dates.

Institutions are expected to maintain capabilities that support efficient clinical trial startup, participant enrollment, and performance monitoring, including streamlined workflows and systems for electronic tracking of milestones. Recipients are encouraged to implement and evaluate approaches that improve trial efficiency and the participant experience.

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), 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://www.congress.gov/bill/119th-congress/house-bill/7148), Division B, Title II, Sec. 224), 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

Not Applicable

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). 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) 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) 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).

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). 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.

5. Evaluation

The success of this NOFO will be evaluated as follows:

1. Is there evidence of research productivity and new knowledge generated on the etiology or underlying biology of EOCs that informs development of novel interventions? Were these findings successfully disseminated?
2. Do funded grants address novel, emerging, or understudied exposures in relation to EOCs?
3. Do funded grants simultaneously address multiple exposures of interest?
4. Do funded grants address a variety of EOCs, including understudied and/or rare cancer types?
5. Do funded grants include representative populations that address differences in the incidence of EOCs by geography or sociodemographic characteristics?

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

Scientific/Research Contact(s)

National Cancer Institute (NCI)
Email: Early-OnsetCancersNOFO_DCCPS_DCB_DCP@mail.nih.gov (mailto:Early-OnsetCancersNOFO_DCCPS_DCB_DCP@mail.nih.gov)

National Institute of Environmental Health Sciences (NIEHS)
Email: NOFO.Information@niehs.nih.gov (mailto:NOFO.Information@niehs.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)
Email: NCIFinancialContact@nih.gov (mailto:NCIFinancialContact@nih.gov)

National Institute of Environmental Health Sciences (NIEHS)
Email: NOFO.Information@niehs.nih.gov (mailto:NOFO.Information@niehs.nih.gov)

Section VIII. Other Information

Recently issued trans-NIH policy notices (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). 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).

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.