

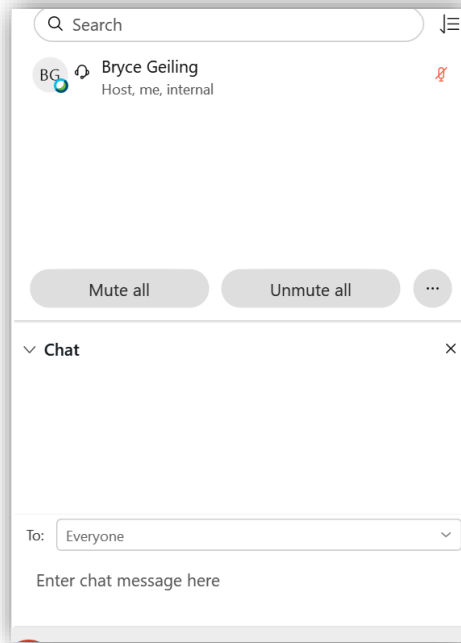
RFA-CA-20-049  
RFA-CA-20-050

# New Cohorts for Environmental Exposures and Cancer Risk (CEECCR; UG3/UH3) & CEECCR Coordinating Center (U24)

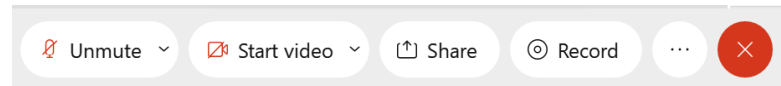
*Pre-Application Webinar, Nov. 10, 2020*

*Somdat Mahabir, Ph.D., M.P.H.*

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# Webinar Presenter



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National Cancer Institute

<https://epi.grants.cancer.gov/staff/mahabir.html>

# Purpose

- RFA CA-20-049 (UG3/UH3) will support approx. 5 new research-based cancer etiology cohorts that use innovative strategies and approaches to address:
  - Gaps between environmental exposures, genetics, and other molecular factors and cancer etiology
  - Ensure rigor and reproducibility by encouraging standardized collection of biospecimen and set of core data across cohorts
  - Racial, ethnic, and geographic disparities
- RFA CA-20-050 (U24) will support a Coordinating Center to facilitate coordination among the new prospective cohorts supported under RFA CA-20-049

# Goal

- Fund approximately five new research-based prospective cohorts:
  - Assess new and understudied exposures with innovative measures
  - Focus on both short-term and longer-term research questions
  - Investigators required to collaborate – facilitated by **Coordinating Center**
  - Priority for the research aims and innovation on methods to achieve those aims – overarching priority on unanswered research questions related to environmental exposures and their public health importance

# Need for New Etiology Cohorts

- Environmental exposures (e.g., new exposures, persistent chemicals, and chemical mixtures) understudied
- IARC and NTP have identified several “Group 1” or “Known Carcinogens” to humans, but many more environmental exposures lack adequate evidence to properly classify
- Identification of the key carcinogenic hallmarks of environmental exposures needed in prospective designs
- Challenge with existing cohorts – aging cohorts; remaining blood samples cannot address current and emerging gaps related to environmental exposures; limited research on life-course exposures; diversity of populations by geography and race/ethnicity

Resources of existing cohorts (data and biospecimens) -- R01/R21/R03 applications

# Short-Term Research Examples

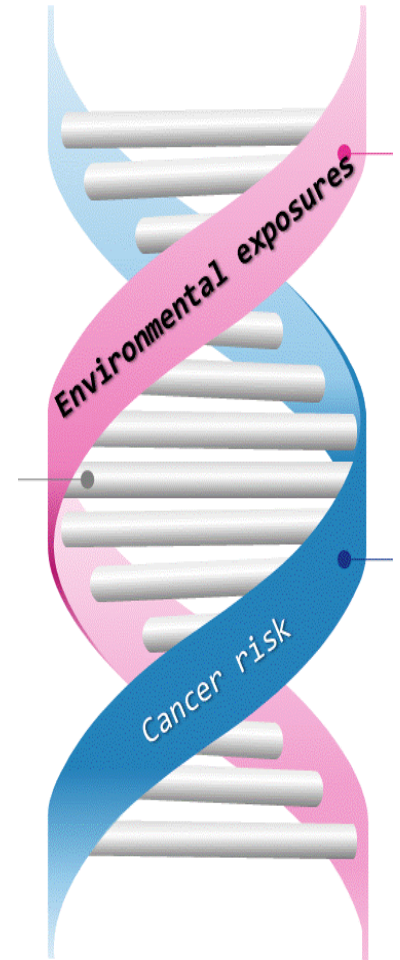
- Use IARC framework to assess biological mechanisms to support classification of environmental exposures
- Other bioassays
- Building new cohorts
- Use incident cases for case-control/case-cohort studies in the initial years

Biological Mechanisms (Carcinogenic characteristics)	Measures
Metabolic activation	DNA and Protein Adducts
Is genotoxic	DNA damage; Gene mutations, Cytogenic changes
Induces chronic inflammation	Elevated WBC; altered cytokine/chemokine production
Is immunosuppressive	Decreased immunosurveillance; immune dysfunction
Alters cell proliferation	Cell proliferation; Angiogenesis

*Smith et al. Key characteristics of carcinogens as a basis for organizing data on mechanisms of carcinogenesis. Env Health Persp 124(6):713-21, 2016*

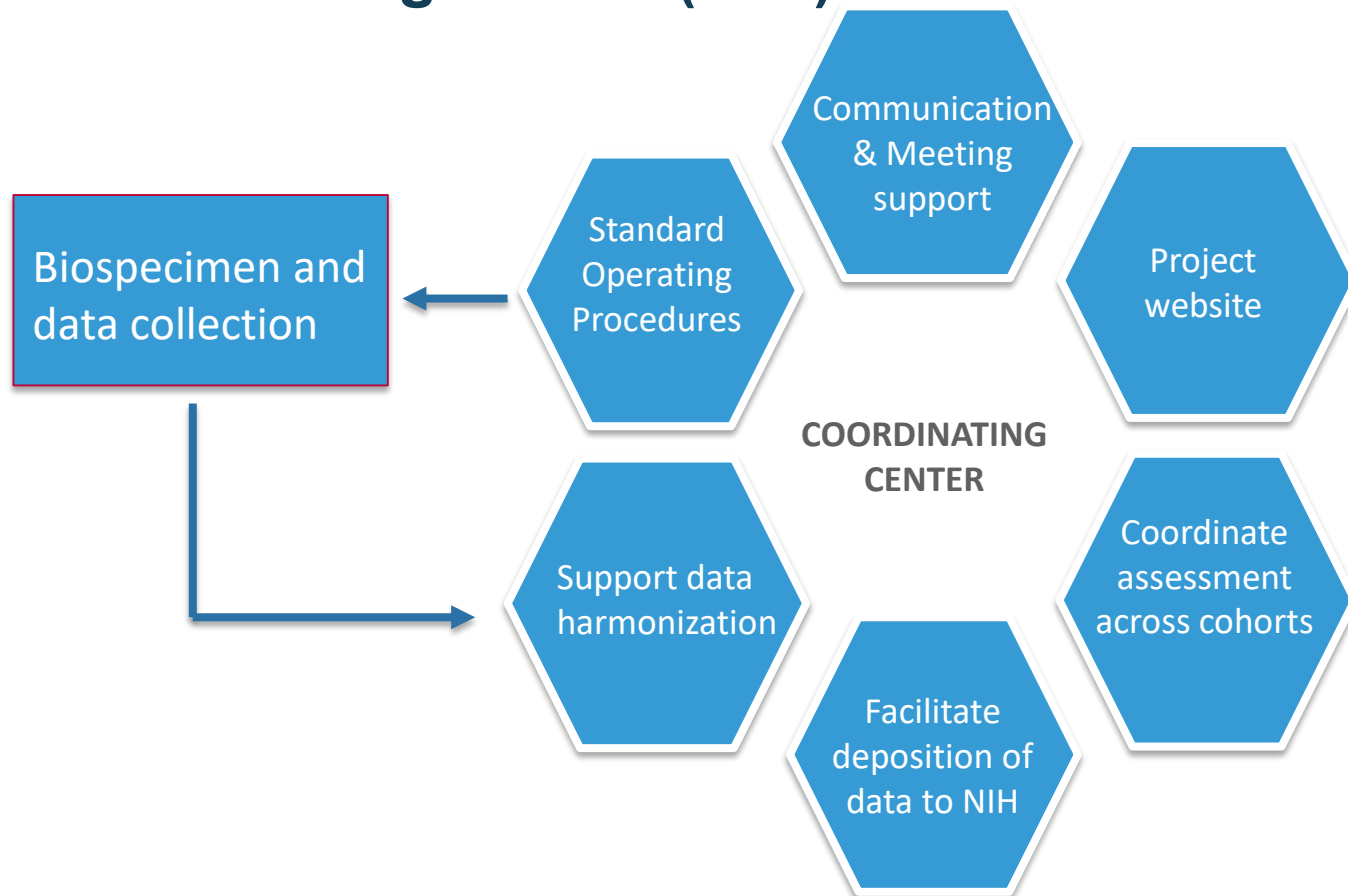
# Longer-Term Research Questions

- What persistent chemicals in the environment affect cancer risk in populations across various geographic areas (e.g. rural, urban)?
- What chemical, physical, lifestyle and genetic factors interact to affect cancer risk in understudied populations?
- How are timing of environmental exposures, multiple exposures, and chronic low-dose exposures associated with cancer development?





# Coordinating Center (U24)



# RFA CA-20-049: Study Requirements for New Cohorts

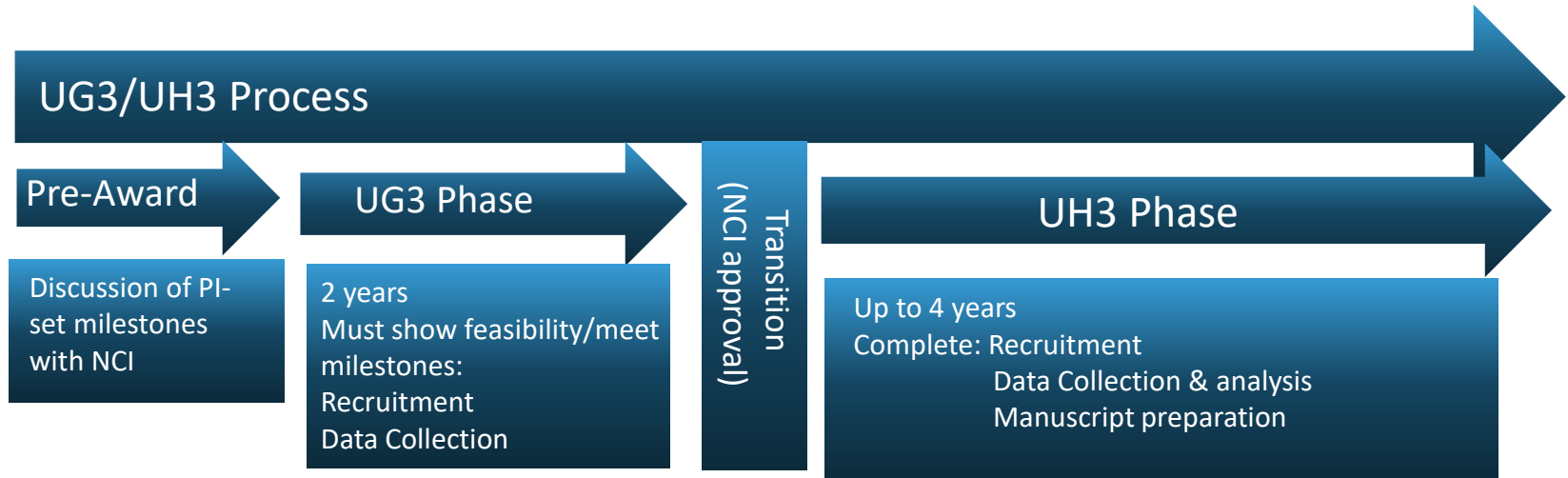
- Scientific justification of the research gaps to be addressed in both exposures and outcomes;
- Evidence of validity and reproducibility of proposed exposure assessments and outcome measures;
- Evidence of community engagement in the development and conduct of proposed research;
- Willingness to collaborate on a core set of data related to environmental exposures and cancer etiology;
- Description of critical milestones, performance metrics, and timeline for completion of milestones;
- Description of sustainability and preservation of cohort resources that extend beyond the life of the award;
- Include data/resource sharing plan.

# RFA CA-20-050: Responsibilities of the Coordinating Center

- The U24 Coordinating Center will operate as supporting infrastructure for the CEECR Program, assisting and supporting the new prospective cohorts under RFA CA-20-049
  - Provide a centralized administrative infrastructure
  - Provide administrative and logistical support for CEECR activities (example, provision of public website for communication)
  - Create standard operating procedures (SOPs) and best practices for the collection of common data/biospecimen elements
  - Facilitate deposition of data to NIH repositories
  - Facilitate communication and meeting support

# UG3/UH3 Research Mechanism

- UG3 phase: PI sets milestones for recruitment and data collection
  - Requires approval from NIH (after selected for funding, before NOA)
  - Cap for UG3 phase: \$750K direct cost for each year in years 1 and 2
- UH3 phase focused on completing research – not guaranteed
  - No cap for UH3 phase: budget must only reflect work needed to accomplish the aims



# UG3/UH3 and U24 are cooperative mechanisms

## These mechanisms facilitate:

- NIH additional involvement
- Additional oversight of awarded grants
- Collaborative work among awardees
- Access of research resource to extramural community
- In-person or virtual meeting in all years

# Non-Responsive Applications (RFA-CA-20-049)

- Approaches that do not include human populations;
- Approaches that are based on secondary use of existing cohort data;
- Approaches that use a study design that will not lead to a prospective cohort;
- Applications from foreign countries that do not show direct relevance to the U.S. population (applications for foreign countries are eligible but must show relevance to U.S. populations); and
- Non-compliant data/resource sharing plans and not following FAIR principles.

# Next Steps

- A recording of the webinar slides and FAQs will be posted to: <https://epi.grants.cancer.gov/cohorts/>
- If you have questions, please contact Somdat Mahabir [mahabir@mail.nih.gov](mailto:mahabir@mail.nih.gov) or Abee Boyles [abee.boyles@nih.gov](mailto:abee.boyles@nih.gov)
- Application due date: January 29, 2021
- Letter of Intent due on December 15, 2020
- Good luck!

## Pre-submitted Questions

### ***How should applications organize specific aims in the UG3/UH3 phases?***

Applicants must provide the overall goals for the entire application and indicate separately Specific Aims to be accomplished in the UG3 and UH3 phases.

### ***Why is NCI funding new cohorts only?***

This RFA for research-driven risk cohorts is responsive to NCAB. Existing cohorts, while important have limitations to address current and emerging gaps related to environmental exposures.



## Pre-submitted Questions

***What are the core set of data and biological specimens to be collected?***

Will be decided at the first annual meeting of the CEECR Program, which will include the cohorts, the Coordinating Center and NIH.

***Can methodological research be built into the cohorts in the short-term?***

Yes.

***What is the population sample size being anticipated?***

Sample size, types and frequencies of biological sample collection will be driven by the science proposed.

## Pre-submitted Questions

***Is the RFA CA-20-049 and RFA CA-20-050 going to be reissued?***

These RFAs currently have one application due date – January 29, 2021.

***Are foreign institutions allowed to apply? What about international partners and/or subcontracts?***

Yes, foreign institutions or studies based in foreign countries are eligible. However, priority will be given to studies with direct relevance to U.S. populations.

# Acknowledgement

- **Planning & Development Team:** Somdat Mahabir, Gary Ellison, Scott Rogers, Joanne Elena, Nonye Harvey, Pothur Srinivas, Kathy Helzlsouer
- **Management Team:** Somdat Mahabir (NCI Lead), Abee Boyles (NIEHS Lead), Curt Dellavalle, Gila Neta
- **Environmental Epidemiology Branch, NCI/DCCPS/EGRP**



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