1. **Who should apply for Open Competition: Environmental influences on Child Health Outcomes (ECHO) Pregnancy Cohort Study Sites. Clinical Trial Not Allowed (UG3/UH3) RFA-OD-22-017?**

Existing ECHO UH3 Pediatric Cohort awardees or subrecipients proposing to recruit new pregnant participants, their resulting offspring, and, if available, the conceiving partner, who did not recruit pregnant participants during the first phase of the ECHO Cohort consortium (2016-2023), should apply to the open-competition RFA-OD-22-017. New applicants proposing to recruit new pregnant participants, their resulting offspring, and, if available, the conceiving partner should also apply to the open-competition RFA-OD-22-017.

2. **Who should apply for Limited Competition: Environmental influences on Child Health Outcomes (ECHO) Pregnancy and Pediatric Cohort Study Sites. Clinical Trial Not Allowed (UG3/UH3) RFA-OD-22-018?**

Existing ECHO UH3 Pediatric Cohort awardees or subrecipients proposing to follow existing ECHO participants AND recruit new pregnant participants, their resulting offspring, and, if available, the conceiving partner, who recruited pregnant participants during the first phase of the ECHO Cohort consortium (2016-2022), should apply to the limited-competition RFA-OD-22-018.

3. **Who should apply for Limited Competition: Environmental influences on Child Health Outcomes (ECHO) Cohort Study Sites for Pediatric Follow Up. Clinical Trial Not Allowed (UG3/UH3) RFA-OD-22-019?**

Existing ECHO UH3 Pediatric Cohort awardees or subrecipients proposing only to follow currently enrolled ECHO Cohort participants should apply to the limited-competition RFA-OD-22-019.

4. **To which RFA should current ECHO awardees apply if they want to recruit new pregnancies and did not do so during the first phase of ECHO (FY2016-2022)?**

They should apply to the open-competition RFA-OD-22-017 (see question 1). If such ECHO awardees also propose to continue to follow existing ECHO participants, they should submit a separate application to the limited competition RFA-OD-22-019.

5. **May prospective applicants apply to follow up an existing cohort of children not funded by ECHO?**

No. ECHO is accepting applications from existing cohorts of children only if ECHO supported them with a UH3 award made under RFA-OD-16-004. However, new applicants proposing to recruit new pregnant participants, their resulting offspring, and, if available, the conceiving partner can apply to the open-competition RFA-OD-22-017.
6. Does ECHO allow an individual to be a PI on applications to more than one Cohort Study Site FOA?

Yes. If applicants choose to do so, they should justify submission of multiple applications and highlight the benefits for the ECHO Cohort consortium. Each application to a FOA should be self-contained and should not overlap in science or budget. Applicants to an ECHO Cohort Study Site cannot also apply to a FOA for an ECHO Core or Center.

7. Will the RFA allow Multiple Principal Investigators (MPIs)?

Yes, multi-PD/PI (MPI) applications are allowed. Please refer to the NIH website http://grants.nih.gov/grants/multi_pi/faq.htm for more information on applying with MPIs.

8. Can applicants propose site-specific analyses and science?

No. These FOAs do not support site-specific analyses and science.

9. How do I budget for personnel for academic activities versus study visits?

Applicants should budget in two distinct major categories. The first major category is for a consistent budget of no more than $375,000 in direct costs per year to support academic activities, including analysis proposal and manuscript development, ECHO committee work, mentoring, and scientific leadership. In this category, applicants may budget for personnel such as the following: PD(s)/PI(s), co-investigators, project managers or coordinators, data managers and analysts, biostatisticians, pre/postdoctoral individuals, and consultants for collaborative intellectual activities. PD(s)/PI(s) must declare a minimum effort of 2.4 person-months (20 percent) per year. The second major category is for a budget proportional to the number of study participants in the proposed plan. This category includes costs related to implementation of the ECHO Cohort Protocol, including but not limited to all field staff needed for tasks related to recruitment, enrollment, retention, and data and biospecimen collection; devices for remote data collection; equipment and supplies; and participant incentives and participant travel.

10. If an applicant proposes more than one Cohort Study Site, can they request $375,000 for each Cohort Study Site to support academic activities, or is $375,000 the total amount that an applicant can request in direct costs per year for academic activities?

The $375,000 in direct costs per year to support academic activities is the total amount per application that an applicant can request. If an applicant proposes more than one Cohort Study Site, they must justify the multi-site structure.

11. Who should pay for the following: Biospecimen kits, shipping of biospecimens, equipment, and proprietary measures?

a. Biospecimen kits – Laboratory Core
b. Shipping of biospecimens to the Laboratory Core – Cohort Study Site
c. Equipment (e.g., scales, stadiometer or tape, iPads, etc…) – Cohort Study site
12. May applicants budget for a biostatistician? Will the Data Analysis Center do all data analyses?

Yes. Applicants may budget for a biostatistician under the category of $375,000 in direct costs to support academic activities. While ECHO anticipates that the Data Analysis Center will do the bulk of data analyses, Cohort Study Sites may propose to perform ECHO Cohort data analyses as well.

13. Is there an estimate on the likely anticipated sample size and budget ranges for each Cohort Study Site?

No, not for each Cohort Study Site. Overall, the ECHO Cohort will consist of approximately 60,000 children. Each Cohort Study Site should propose a budget based on their anticipated sample size and the guidelines provided in Section IV of the FOA:

14. Should applications include only a single Cohort Study Site?

The NIH ECHO Program Office encourages each applicant to submit only one Cohort Study Site application. If an applicant includes more than one Cohort Study Site in their application, they must justify the multi-site structure.

15. What is the ECHO Cohort? How does it differ from the “ECHO-wide Cohort?”

ECHO investigators from the first phase of the ECHO Cohort Consortium (2016-2023) established the ECHO Cohort by combining data and biospecimens from multiple pre-existing and ongoing maternal-child cohort studies, driven by the ECHO Cohort Protocol. In the next phase (2023-2030), ECHO investigators will continue to populate the ECHO Cohort data platform through newly collected data and biospecimens.

“ECHO Cohort” will replace the current term, “ECHO-wide Cohort.”

16. What are the five key ECHO outcomes?

ECHO’s five pediatric outcome areas are pre-, peri- and postnatal, upper and lower airways, obesity, neurodevelopment, and positive health.

17. What is positive health, one of the five ECHO child health outcome areas?

Positive health refers to “health assets (biological, functional, behavioral, and experiential) that strengthen an individual’s capacity to adapt, satisfy needs, and fulfill goals.”
Conceptually, the positive health approach refers to studying “what goes right” rather than “what goes wrong.” Within ECHO, to date we have operationalized the positive health outcome not as the absence of disease, but rather as well-being, consisting of one or more of global health, life satisfaction, positive affect, and meaning & purpose. These are core elements within the ECHO Cohort Protocol. Other researchers have suggested including physiological, physical, or other psychological constructs within the positive health domain. Within the ECHO perspective, brain, body, and environmental assets, e.g., sleep health and physical activity, are on the pathway to positive health (as well as other ECHO child health outcomes) and are not part of the positive health outcome itself.

18. What does ECHO mean by Cohort Study Site?

The Program Office defines an ECHO Cohort Study Site as an institution at which participant recruitment and follow up takes place at one or multiple locations, e.g., the Cohort Study Site could be a medical system with recruitment taking place at its clinics.

19. What is a specialized exposure or outcome area? What are core and specialized data elements?

The Specialized Exposure areas that Cohort Study Sites recruiting new pregnant participants can propose are a) Physical & Chemical, e.g., air pollution and household chemicals; b) Lifestyle, e.g., nutrition, sleep, and physical activity; or c) Psychosocial, e.g., stress, social support, and discrimination. Specialized Outcome areas include ECHO’s five key child health outcomes area: pre-, peri- and postnatal, upper and lower airways, obesity, neurodevelopment, and positive health.

Specific Aim 2 should incorporate question(s) that leverage proposed specialized exposure and/or specialized outcome areas.

Applicants may propose specialized data elements to support those specific aims. Core data elements – data elements and biospecimens that every Cohort Study Site will collect on every participant. For the purposes of applying to this FOA, consider all elements in the Draft ECHO Cohort Protocol (v3.0) core.

Specialized data elements - more frequent or more detailed elements than the Core elements. ECHO anticipates that the Steering Committee will add specialized elements to the ECHO Protocol during the UG3 phase. Within their specialized area(s), each Cohort Study Site will collect every specialized element on every participant.

20. Which applicants need to propose both specialized exposure areas and specialized outcome areas?

Applicants responding to either RFA-OD-22-017 or RFA-OD-22-018

21. Which applicants need to propose only specialized outcome areas?

Applicants responding to RFA -OD-22-019
22. When will ECHO Cohort Study Sites begin collecting core data and biospecimens? Specialized data and biospecimens?

ECHO anticipates that Cohort Study Sites will begin collecting core elements in the first grant year of the study period, and Steering Committee-approved specialized elements in the second year.

23. Does a Cohort Study Site need to collect all core data elements at every visit?

No. The schedule for collecting all core data elements distributes over several years.

24. Will Cohort Study Sites need to collect data on all 5 key health outcomes?

Yes. The core data elements of the ECHO Cohort Protocol will include all 5 key health outcomes. Applicants to any of the three Cohort Study Site FOAs (RFA-OD-22-017, RFA-OD-22-018, RFA-OD-22-019) should propose one of the five outcome areas as a Specialized Outcome area.

25. Can applicants propose biospecimen assays?

Yes. Applicants may propose biospecimen assays that the Laboratory Core is likely to support, which may include targeted assays of single chemicals or panels; untargeted exposomics and metabolomics; microbiome analysis; genetics, epigenetics, or other ‘omics; biological response indicators. Please see Laboratory Core RFA-OD-22-016 for details.

26. When will the ECHO Cohort recruit participants into the preconception pilot?

The ECHO Cohort will recruit 20,000 pregnant participants. Derived from the postpartum period of these 20,000 pregnant participants, the ECHO Cohort will include a preconception pilot study of approximately 10,000 potential pregnant participants and, if available, their conceiving partners who are at moderate to high probability of having a subsequent child during the study period (FY2023-2030). ECHO anticipates that the Cohort Consortium will develop and implement a Steering Committee-approved preconception phase of the ECHO Cohort Protocol within the first year of the study period.

27. Do Cohort Study Sites need to complete recruitment during the UG3 phase?

No. Recruitment will take place in the UH3 period as well.

28. What do the ECHO FOAs mean by diverse populations?

In these FOAs, the term "diverse populations" includes health disparity populations as defined by NIH.

29. Can Cohort Study Site applicants propose to recruit participants living in foreign (non-U.S.) countries?

No. While the RFA does allow applicants to include foreign components in their applications, the ECHO Program Office will not allow Cohort Study Sites to recruit participants living in foreign (non-U.S.) countries.