ECHO-wide Cohort Ancillary Study Policy

I. Introduction

Investigators are encouraged to propose ancillary studies to advance the mission of the Environmental influences on Child Health Outcomes (ECHO) program. ECHO-wide Cohort Ancillary studies ("ancillary studies"), using non-ECHO funding, will expand the efforts already underway through the ECHO program.

The ECHO program aims to understand the effects of environmental exposures on child health and development. The design of ECHO will capitalize on existing participant populations, and support approaches that can evolve with the science and take advantage of the growing number of clinical research networks and technological advances.

II. Purpose

The purpose of this policy is to describe how the ECHO Ancillary Study Committee, Publication Committee and Steering Committee review and approve ancillary studies.

- Ensure appropriate use and availability of ECHO resources
- Ensure budgetary plans are adequate to support ancillary study activities
- Confirm proposed ancillary studies do not conflict with or duplicate work underway within the ECHO program
- Encourage equality, transparency, and fairness in decision-making processes related to the development of ECHO research products

III. Scope

This policy applies to all ECHO-wide Cohort ancillary studies. The ECHO Coordinating Center (CC) will provide the overall coordination and support of activities and communications for the review of ECHO-wide Cohort ancillary studies.

IV. Definitions

Item	Description
Ancillary Study Concept	A formal request to inform the ECHO scientific community about an ancillary study idea.
Ancillary Study Proposal	A formal request submitted by investigator(s) to use ECHO resources to answer scientific questions that require additional resources beyond those provided by ECHO.

Item	Description
Ancillary Study Committee	The Ancillary Study Committee is the body that upholds the ECHO Ancillary Study Policy and is involved in the initial programmatic/feasibility review of an ancillary study.
ECHO Publication Committee	The governing body that upholds the ECHO Publications Policy.

V. Policy

A. Definition of an Ancillary Study

An ECHO Ancillary Study includes any study that derives funding from a non-ECHO source and uses non-publicly available data or biospecimens collected by more than one ECHO award under the ECHO-wide Cohort Data Collection Protocol. The ancillary study may also collect new data or biospecimens from ECHO-wide Cohort participants.

B. Funding

The investigator proposing the ancillary study must provide, where appropriate, all funding for all proposed bioassays, ancillary study procedures including additional activities by the Data Analysis Center (DAC), CC, Person Reported Outcomes (PRO) Core, and ECHO Cohort Awards. Ancillary studies cannot use ECHO funding for any activities.

C. Requirements for Approval

Approval requires that an ancillary study will support the ECHO program aims to understand the effects of environmental exposures on child health and development and will not:

- interfere with the completion of the main objectives of the ECHO-wide Cohort Data Collection Protocol
- adversely affect participant cooperation in compliance with the ECHO-wide Cohort Data Collection Protocol
- jeopardize the public image of the ECHO program
- be duplicative of efforts already underway either through the ECHO program itself or through other proposed ancillary studies
- commit resources/effort supplied by the CC, DAC, PRO Core or study cohorts to complete the aims of the ancillary study until they are discussed with the Principal Investigators from Components and are included in the budget of the ancillary study

D. Ancillary Study Committee

The Ancillary Study Committee will include representatives from each of the following ECHO components:

- Coordinating Center (1)
- Data Analysis Center (1)
- Patient Reported Outcomes Core (1)
- Human Health and Exposure Analysis Resource (HHEAR) (1)
- ECHO cohorts (4)
- National Institutes of Health (NIH) (1; non-voting)

The ECHO Ancillary Study Committee is responsible for maintaining and upholding the *ECHO-wide Cohort Ancillary Study Policy*. The Ancillary Study Committee will conduct initial feasibility reviews (screenings) of ancillary study concepts. This initial review can occur prior to full development of an ancillary study proposal to avoid effort by the ancillary study team for a study that is infeasible within ECHO. Full review of an ancillary study proposal requires a complete assessment for feasibility by the Ancillary Study Committee and review by the ECHO Publication Committee for scientific merit and consideration of any duplication of efforts with analyses that are underway.

The ECHO Steering Committee gives final approval of the ancillary study proposal, based on the recommendation of the Ancillary Study Committee.

E. Requirements of Investigators

At a minimum, one ECHO Principal Investigator (PI) must be included as a co-investigator of an ancillary study proposal. If the ancillary study PI is not an ECHO PI, the ancillary study PI will collaborate with the ECHO PI, to prepare the ancillary study proposal, its submission to the Ancillary Study Committee, and subsequent communications.

F. Requirements of Institutions

Investigators who plan to propose an ancillary study must conduct the study at an institution that meets the following requirements:

- access to institutional review board (IRB) that complies with applicable USA Federal regulations governing research involving human subjects.
- ability to maintain documentation of completion of research ethics training by all research team members who work with ECHO data and/or biospecimens.
- registration with Dun and Bradstreet and provision of the Data Universal Numbering System Number or DUNS number.

G. ECHO Conflict of Interest

All Investigators listed in an ancillary study proposal must comply with the *ECHO Conflict of Interest Policy* and submit the *ECHO Conflict of Interest Form* with the ancillary study proposal

going for full committee review. The form is located on the ECHO SharePoint site https://flow.dcri.org/sites/echo/conflict-of-interest/SitePages/Home.aspx. Any additional Investigator added after approval of an ancillary study proposal must also complete a Conflict of Interest (COI) form.

H. Completion of Ancillary Study Concept and Proposal

Investigators are encouraged to complete an ancillary study concept if they would like to obtain feedback on feasibility and/or gauge interest from components associated with ECHO. The appropriate ECHO components (i.e., CC, DAC, ECHO biorepository, HHEAR or PRO Core) review the completed ancillary study concept and provide feedback (i.e., budget, data or biospecimen availability, feasible/ not feasible, etc.) to the ancillary study PI. To apply for review of an ancillary study concept, investigators complete and submit an electronic written request via the ECHO ancillary study concept form. After an affirmative feasibility review of the ancillary study concept, the next step is to submit an ECHO ancillary study proposal for review.

To apply for full review and approval of an ECHO ancillary study, investigators complete and submit an electronic written request via the ECHO ancillary study proposal form.

All resources to comply with ECHO ancillary study processes and procedures are located in the ECHO SharePoint site. Information on the site includes ECHO policies, *ECHO Manual of Procedures* (MOP), *Data Use Agreements* (DUA), how to set-up an account for access to the ECHOPortal, training information, data and biospecimen collection information.

1. **Timeline**

   For an initial feasibility review, the ECHO CC circulates the ancillary study concept to the appropriate ECHO components for review and subsequent review by the Ancillary Study Committee. The feasibility review of an ancillary study concept by the ECHO components takes up to 10 business days.

   The ECHO Ancillary Study Committee completes the review of the ancillary study proposal, including assessment by the Publication Committee, within 20 business days. ECHO Steering Committee review occurs at the next scheduled Steering Committee meeting following the full review of the Ancillary Study Committee.

2. **Consent and IRB Approval**

   Consenting and study conduct must conform to Good Clinical Practice (GCP) guidelines and information outlined in the ECHO MOP. Ancillary study investigators must include in their ancillary study proposal details about informed consent, if applicable, including plans for communicating with the participants of the ancillary study. The proposal must also note if involvement of the ECHO single IRB (sIRB) is required. Investigators are required to ensure confidentiality of individual identifiable data for ancillary study participants. Investigators must ensure that the use and disclosure of Protected Health Information (PHI) obtained under their protocol complies with the Health Insurance Portability and Accountability (HIPAA) Privacy Rule. Investigators must comply with the *ECHO Individual Return of Research Results Policy* and the *ECHO Data Sharing Policy*.

Complying with these policies impacts the information that must be conveyed during informed consent. Specifically, a participant must agree to return of results in order to return results to the participant; and the participant must agree to sharing of data and/or biospecimens from an ancillary study linked to other data collected and shared by ECHO in order to share these data and/or biospecimens.

After the investigator receives a notice of funding, if the ancillary study involves human subjects research, the ECHO CC requires documentation of IRB approval. For projects not involving human subjects' research or for exempt research, the ECHO CC requires documentation of IRB consultation or determination that the research is not human subjects' research or qualifies as exempt.

Prior to study implementation, the investigator must send copies of the following documents to the ECHO CC (echocc@dm.duke.edu): award notification; IRB documentation including approval of exempt status; the final research protocol with documentation of IRB approval, if applicable; and informed consent documents, if applicable.

3. Data Access and Management

Ancillary study investigators must include in their ancillary study proposal a plan for using ECHO-wide Cohort data and sharing data collected or generated under the ancillary study or state appropriate reasons why such sharing is restricted, not possible, or not relevant. ECHO-wide Cohort data access and management information is located in the ECHO MOP. Investigators must comply with the *ECHO Data Sharing Policy*. Sharing may only occur under terms and conditions consistent with informed consent provided by individual participants, and as approved by the oversight IRBs and any local, state and USA Federal laws and regulations. Ancillary study investigators are encouraged to share data collected or generated under the ancillary study via ECHOPortal maintained by the DAC with appropriate consideration of costs associated with documentation, storage, access, and maintenance of the data and tools required for use of the data in data analysis and visualization. The ancillary study is responsible for all costs associated with data access and management.

4. Biological Sample Access

The ECHO Biorepository will provide requested biospecimens to the investigator for each approved ancillary study. Ancillary study investigators must include in their ancillary study proposal a plan for the use of biospecimens requested from the biorepository in accordance with the ECHO MOP, *ECHO Biospecimen Utilization Policy* and the *ECHO Biospecimens Collection Processing & Storage Policy*. The plan will include justification for the use of biospecimens from the biorepository and/or any collection of new biospecimens. If it is anticipated that there will be any residual from newly collected biospecimens, the plan will describe how they will be shared or state appropriate reasons why such sharing is restricted, not possible, or not relevant. The plan will also include a detailed breakdown of costs associated with the use of biospecimens from the biorepository. The ancillary study is responsible for all costs associated with the use of biospecimens.

This will include costs associated with the following activities:

- the DAC identifying biospecimens consistent with the study design.
- the DAC developing a pull list for the biorepository.
- the biorepository pulling and shipping biospecimens.
- the DAC developing any necessary design documents for the laboratory to receive and analyze the biospecimens,
- the DAC maintaining tracking documents and incorporating laboratory results back into the ECHO-wide Cohort database when the laboratory analysis is complete.

Sharing may only occur under terms and conditions consistent with informed consent provided by individual participants, and as approved by the oversight IRBs and any local, state and USA Federal laws and regulations. Collecting new or using archived biospecimens will receive careful consideration to ensure current and future ECHO objectives have adequate amounts of biospecimens available for analysis. All ancillary study proposals must include a clear explanation of the type and quantity of material required including justification of the amount. This will be a consideration of the Publications Committee review.

5. **Data Management and Statistical Support**
   An ancillary study proposal must include adequate plans for data management and statistical support. The plan must state if data management and statistical analyses will be completed by the investigator, by the ECHO DAC, or by another party. The plan may need to include consideration of costs associated with set-up by DAC staff for access and use of data and resources on ECHOPortal, including training, execution of data use agreements, assignment of user IDs and passwords, designation of workspace, provision of compute time, and access to relevant tools/software. Additional DAC resources may be required in the development of questionnaires and data capture instruments; the development of tools for data analyses, visualizations, and collaborations; and the design and analysis of ancillary study data linked to ECHO-wide Cohort data. Data transfers from HHEAR or other laboratories need to be included in the Data Management and Support plan. The ancillary study is responsible for all costs associated with data management and statistical support.

6. **Data Ownership and Sharing**
   The *ECHO Data Sharing Policy* outlines how to make new data collected or generated as part of an ancillary study available to the ECHO research community.

I. Approval Process

An ancillary study proposal **must receive approval from the ECHO Ancillary Study and Steering Committees before submitting a grant to conduct the study.** After review of the ancillary study proposal, investigators will receive written notice of the recommendation/feedback of the ECHO Ancillary Study and Steering Committees. After approval of an ancillary study, the Investigator must submit any changes in scope or procedures to the ECHO Ancillary Study and Steering Committees for review and approval.

1. Ancillary study proposals receive one of the following after review:
   - **Approve:** The CC communicates this decision to the investigator.
   - **Not approve:** The CC communicates this decision to the investigator. The CC will provide comments from the review to the study team. In some instances, the investigator may be able to address concerns of the reviewer, revise the proposal, and resubmit.
2. Resubmission of Ancillary Study Proposals
   After approval of an ancillary study proposal, the CC will enter the proposal into the ECHO ancillary study database maintained by the ECHO CC. Once approved, ancillary studies have two (2) years to receive funding. After two years, if a proposal does not receive funding it is marked as "withdrawn" and marked inactive. After 2 years, if the original investigator wants to continue to pursue the project, they must submit a new ancillary study proposal for review, with an explanation about reactivation of the project. If the initial submission to a funding agency is unsuccessful and the PI submits the ancillary study proposal as a revision application or for a subsequent funding opportunity, they must communicate this to the Ancillary Study Committee. The investigator will provide a description of any changes to the original study plan to the Ancillary Study Committee who may determine a re-review is necessary based on the nature of the changes.

J. Annual Progress Report

The ancillary study investigator must keep the ECHO CC informed of major developments in the life of the ancillary study proposal or study, including success of funding the application, start/end dates, changes in protocol, and any resulting publications or presentations. Investigators conducting ancillary studies are responsible for submitting annual progress reports once the study has initiated and until the study has been closed-out. To inform the ECHO program, the investigator submits a progress report annually to the ECHO CC, which will be included in applicable reports (NIH RPPR, ECHO updates or newsletters, etc.). A shell document for reports is located on the ECHO ancillary study website.

K. Publication and Presentations

Any publication of data from ECHO participants originating from an ECHO ancillary study must adhere to the *ECHO Publications Policy* and approved by the ECHO Steering Committee following those procedures outlined in the *ECHO Publications Policy*. PIs, investigators, and/or research team members of the ancillary study will act as writing team leads for proposed publications. This procedure is necessary to establish authorship and prevent overlap in the publication effort.

VI. Review and Revision

All ECHO Program Manual documents are to be reviewed at least every two years; however, more frequent review may be warranted as processes change or major edits are identified.

VII. Supporting Documents

ECHO Analysis Study Concept Form
ECHO Analysis Study Proposal Form

VIII. References

ECHO-wide Cohort Data Collection Protocol
ECHO Manual of Procedures (MOP)
ECHO Conflict of Interest Policy
ECHO Individual Return of Research Results Policy
ECHO Publications Policy
ECHO Biospecimen Utilization Policy
ECHO Biospecimens Collection Processing & Storage Policy
ECHO-wide Cohort Data Sharing Policy

IX. Attachments

Attachment A - ECHO Ancillary Study (AS) Flow Chart

X. History of Change (Since Last Version)

Section Affected	Version Date	Changes Made
N/A	01/Oct/2021	New Policy

Approval Page

Name/Title	Signature/Date
ECHO Steering Committee	October 1, 2021 (via electronic vote)

Attachments

Attachment A - ECHO Ancillary Study (AS) Flow Chart