ECHO Cohort Ancillary Studies Policy

I. Introduction and Purpose

The scientific impact of the ECHO Cohort relies upon the availability of its data and biospecimen resources, to which ECHO provides access in two ways: 1) with limited personally identifiable information (PII) on the ECHO Cohort Data Platform (Data Platform) — a highly secure, FISMA-moderate compliant cloud environment, along with the biospecimens in the ECHO Biorepository; and 2) de-identified, controlled-access, public-use datasets—currently located on the *All of Us* Researcher Workbench — available to the broader scientific community. Learn more about using ECHO public-use datasets here: https://echochildren.org/data-availability/

The scientific community may take advantage of ECHO data with limited identifiers, including proposing new assays of biospecimens, by proposing ancillary studies. **The ECHO Cohort Consortium defines an ancillary study as one that derives funding from a non-ECHO source—like other NIH grants, non-federal grants, or institutional funds—and accesses non-publicly available, limited identifiable data on the Data Platform, and biospecimens in the Biorepository**.

The purpose of this policy is to govern the process for proposing ancillary studies.

II. Scope

This policy applies to any individual or institution proposing an ancillary study supported by non-ECHO funding that seeks access to:

A. ECHO Cohort data (with limited PII) *only*

B. ECHO Cohort biospecimens and associated data (with limited PII)

Note: This policy does *not* currently allow requests for access to ECHO Cohort participants, including for piloting new methods or new data or biospecimen collection in addition to the *ECHO Cohort Data and Biospecimen Collection Protocol*.

CRITERIA

The first criterion for ECHO ancillary studies is whether the studies require support from non-ECHO funding. If so, the second criterion is whether the studies require use of ECHO Cohort biospecimens or data with limited identifiers on the ECHO Cohort Data Platform. If the proposed study does not require access to the limited identifiers on the Data Platform or ECHO's biospecimens, then the controlled-access, public-use data from the ECHO Cohort located on the

All of Us Researcher Workbench may be appropriate. If so, the investigators can submit a request to access the requisite data using the *All of Us* Researcher Workbench access request system.

If the study meets both criteria, (1) requiring non-ECHO funding and (2) requiring access to ECHO Cohort data with limited identifiers or biospecimens, then the study may be ancillary and can proceed only in accordance with the policy below.

III. Definitions

Refer to the ECHO Glossary for full list of ECHO terminology and definitions.

IV. Policy

NIH and the ECHO Cohort Steering Committee (Steering Committee), or a sub-group they appoint, must review all ancillary study proposals promptly and, if they approve it, provide a Letter of Collaboration to the ancillary study investigator.

Access to the ECHO Cohort's limited identifiable data on the Data Platform or biospecimens for an ancillary study are contingent upon the investigators obtaining or adhering to the following elements, each described in the subsections below.

- Institutional Review Board (IRB) documentation
- Letter of Collaboration from the ECHO Cohort Consortium
- Non-ECHO funding
- An ECHO X01 award for resource access, if needed
- Official training and certification from the ECHO Cohort Consortium cores and centers
- Adherence to the ECHO Cohort Data Sharing and Use Policy, ECHO Cohort Biospecimens Policy, ECHO Cohort Publications Policy

A. Institutional Review Board (IRB) Documentation

All investigators applying for an ECHO Ancillary Studies Letter of Collaboration must attest that their IRB is responsible for either

- For ancillary studies using biospecimens: approving the study design, or
- For data-only ancillary studies: Consideration of exempting them from human subjects research protections

The appropriate IRB may be the investigators' local institutional IRB or single IRB overseeing their research arising from their source(s) of funding.

Prior to beginning their ancillary study, investigators must provide the ECHO Coordinating Center with documentation of their IRB's determination of study approval or exemption. If the documentation is not on file, the ECHO Cohort Consortium may pause or restrict the investigators' access to any or all ECHO data or biospecimen resources.

B. Letters of Collaboration from the ECHO Cohort Consortium

Consistent with NOT-OD-26-094, ECHO is now offering Letters of Collaboration instead of the Letters of Support provided previously. Prior to applying for non-ECHO funding or an NIH ECHO X01 (see Section IV part D. below), every ancillary study proposer must request a Letter of Collaboration from the ECHO Cohort Consortium. The applications for non-ECHO funding and the ECHO X01 for the ancillary study must each include this Letter of Collaboration.

The Consortium's Letters of Collaboration are not explicit promises of resource access but serve as confirmation that project proposals meet all the criteria of an ancillary study of the ECHO Cohort and are feasible with the Consortium's data and biospecimen resource inventories and support infrastructure. Once funding and, if applicable, X01s are secured, the Consortium requires investigators to submit analysis proposals that complement their project descriptions for which they received their letters, through the ECHO Cohort Consortium's analysis pipeline.

To begin the Letter of Collaboration Request process, proposers must first submit their study summary to the NIH ECHO Program Office during an open period. Learn more at https://echochildren.org/-echo-ancillary-studies/. If the NIH ECHO Program Office approves based on the overarching criteria aligned with PAR-25-437, the proposer can submit the full request form to the ECHO Cohort Consortium according to the instructions on https://echochildren.org/request-a-letter-of-collaboration/. If not, the requester can modify the proposal and try again in a future round.

Letters of Collaboration issued by the ECHO Cohort Consortium are good for use in funding applications for two years. After expiration, Letters of Collaboration for data-only projects can be reissued through a brief request submitted using a link on https://echochildren.org/echo-ancillary-studies/. Letters of Collaboration for projects that involve use of biospecimens must start the full request process anew to account for potential changes in biospecimen availability in the ECHO Biorepository.

C. Non-ECHO funding

ECHO ancillary studies require support from non-ECHO funding sources. In addition to funding to cover ancillary study-site staff time, resources, and training, the funding must provide adequate support for the ECHO Cohort Consortium cores and centers (e.g., Coordinating Center, Data Analysis Center, Laboratory Core) for the duration of the ancillary study period. Learn more about budgets at https://echochildren.org/request-a-letter-of-collaboration/.

If investigators are submitting a funding application to support the Ancillary Study, investigators must notify ECHO.NOFO@nih.gov at the time of submitting their funding application to provide the relevant tracking information, including RFA or NOFO identifier, application identifiers, and contact PI name.

To prevent delays in ancillary study projects, investigators must notify as soon as possible ECHO.NOFO@nih.gov, echocc-ancillarystudy@duke.edu, and echo-help@rti.org (and elvis_pub@vumc.org if projects include biospecimens) of funding application outcomes, including intent to reapply if funding was unsuccessful.

D. Application for resource access through an ECHO X01

ECHO requires investigators to apply for an NIH ECHO X01 award in two scenarios.

1. Investigators who are not currently funded as part of the ECHO Cohort Consortium must apply for an NIH ECHO X01 award.
2. ECHO-funded investigators who seek to use ECHO biospecimens for an ancillary study must apply for an NIH ECHO X01 award.

   Note: ECHO investigators do not need an X01 award for data-only ancillary studies.

The ECHO X01 is a resource access mechanism that allows NIH oversight of the ancillary study (see Section IV part G below). The ECHO X01 does not provide funding.

All ECHO resource access applications must include the Letter of Collaboration from the ECHO Cohort Consortium obtained according to Section IV part B of this policy. If applying for non-ECHO funding to support their ECHO ancillary study, investigators must simultaneously (or as close to simultaneously as possible) apply for an ECHO X01. If investigators already have funding in hand, they must still apply successfully for an X01 before beginning their ancillary study.

E. Restrictions

Off-cycle requests for Letters of Collaboration

This policy does not permit off-cycle requests for Letters of Collaboration from the Consortium. Investigators can request letters through the official process and timelines described on https://echochildren.org/echo-ancillary-studies/ and https://echochildren.org/request-a-letter-of-collaboration/.

Modifications to projects with Letters of Collaboration

Once a Letter of Collaboration is issued for a project, this policy precludes any changes to project title, project aims, or PI listed in consortium records. If investigators need to change their project title, aims, or PI, they must request a new letter through the official process.

Access to ECHO Cohort participants

This policy excludes study proposals seeking access to ECHO Cohort participants. ECHO investigators seeking access to ECHO Cohort participants for the purposes of piloting new methods, new data collection, or potential changes to the *ECHO Cohort Data and Biospecimen Collection Protocol* can apply to the ECHO Opportunities and Innovation Fund.

Project timelines

ECHO expects timely completion of all ancillary studies, within reason. For example, investigators should complete data-only ancillary studies within two years of submitting the initial analysis proposal through the Consortium's data analysis pipeline. For projects involving use of biospecimens, investigators should complete the ancillary studies within three years of submitting the initial analysis proposal through the Consortium's data analysis pipeline.

F. Exemptions

If ECHO Cohort Study Sites, Cores, or Centers sponsor training award applicants (e.g., to F or K awards), the investigators in training can propose their training projects as *data-only* ECHO Cohort ancillary studies. Sponsors must be an investigator (i.e., Principal Investigator, or Co-investigator) listed on an ECHO Cohort Consortium Study Site, Core, or Center grant application as "key personnel" and who draws salary support from an active ECHO Cohort Consortium Study Site, Core, or Center award.

Principal investigators of such training projects should request Letters of Collaboration for their ancillary studies *prior* to their training award application submissions, so that they can attach their Letter of Collaboration to their applications.

Given the limited budget for most training awards, ECHO Cohort Consortium sponsors should identify a project data analyst who will undergo, or who has previously completed, training and certification required for ancillary studies by the Data Analysis Center. Alternatively, training award principal investigators may serve as project data analysts and undergo the training and certification by the Data Analysis Center.

Training award applicants requesting Letters of Collaboration for *data-only* ancillary studies are exempt from both

- Proposing ancillary study budgets to support ECHO cores or centers
- Applying for an ECHO X01

Note: The exemptions above may not apply to K99/R00 awards. Applicants to K99/R00 awards should check with the NIH ECHO Program Office about possible exemptions.

G. NIH Oversight

The NIH ECHO Program Office provides oversight of all ECHO ancillary studies through ECHO "U" awards and/or the X01. All ECHO awardees, including X01 awardees, must abide by all NIH policies as well as the ECHO Cohort Data Sharing and Use Policy, ECHO Cohort Biospecimens Policy, and ECHO Cohort Publications Policy.

To help NIH ensure the responsible conduct of ECHO's research—including ancillary studies—the X01 requires ancillary study investigators

- Assure proper training and certification of their site staff to access and use ECHO Cohort resources.
- Provide reports to NIH ECHO Program staff, the ECHO Coordinating Center, the ECHO Data Analysis Center, and the ECHO Laboratory Core, as needed or when requested, regarding X01 award site activities, including but not limited to, staff training and certification, summaries of ancillary study progress and outputs.
- Protect the confidentiality of participants, promote ethical and beneficial use of data among data users, and minimize potential harms to people groups or individuals.

- Complete their projects within the two- or three-year timelines, as specified in Section IV Part D, above. While some flexibility is available for reasonable delays, NIH can issue restrictions to data and biospecimen access for investigators with overdue projects.

H. Disputes and Appeals

Investigators may dispute Consortium decisions about ECHO ancillary studies. The Steering Committee or ECHO Cohort Operations Committee hears such appeals.

If an appeal remains unresolved after Steering Committee or Operations Committee hearings, consortium members may ask the ECHO Program Office to convene a Dispute Resolution Committee.

To initiate an appeal, investigators should email ECHO.NOFO@nih.gov and echocc-ancillarystudy@duke.edu notifying them of the decision of concern and the desire to appeal.

V. Review and Revision

Review of ECHO Program Manual documents occurs every three years; however, as processes change, or major edits identified, this may warrant additional review of documents.

VI. Supporting Documents

None

VII. References

- NICHD Data and Specimen Hub (DASH)
- NIH Guide
- ECHO Opportunities and Innovation Fund
- Notice: NIH is replacing Letters of Support with Letters of Collaboration (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-26-094.html)

VIII. Attachments

ECHO Cohort Ancillary Studies Process from Applicant Perspective.

IX. History of Change

Version Number	Effective Date	Section Affected	Summary of Changes
3.0	24Sep2026	See Below	
		Throughout	Editorial revisions
		II	The criteria for an ancillary study was moved from Section IV.A to Section II
		IV.A	The section includes policy directives for IRB documentation
		IV.B	This section now includes info on Letter of Collaboration durations and needed actions when they expire
		IV.C	The section includes new policy directives requiring ancillary studies investigators to notify NIH and Cores/Centers of funding application tracking info and outcomes
		IV.E	The section now includes new policy directives officially restricting off-cycle reviews and revisions to projects that already have a Letter of Collaboration. This section also includes restrictions on ancillary study timelines.
		IV.G	Edits in this section clarify that all ancillary study investigators are responsible for adhering to all NIH policies and pertinent ECHO policies. This section now includes ramifications for unreasonably delayed ancillary studies.
		Attachments	Removed the graphic of the ancillary studies process overview. For details, see graphics on https://echochildren.org/-echo-ancillary-studies/
2.0	02Jul2025	Entire Policy	Revised policy to support ECHO Cycle 2.
1.0	01Oct2021	N/A	New Policy

Approval Page

Name/Title	Approval Date
NIH ECHO Program Office	25Sept2026