ECHO Biospecimen Utilization Policy

I. Introduction

Under direction from the Environmental Influences on Child Health Outcomes (ECHO) Steering Committee, this policy directs the utilization and management of the ECHO Biospecimens collected by all ECHO Cohorts.

II. Purpose

This policy balances two important goals: to facilitate investigations of the impacts of a broad range of early environmental exposures on pediatric health and, at the same time, to respect and protect the participants whose biospecimens have been contributed by the ECHO Cohorts to the ECHO Program. This policy seeks to ensure that investigators use existing and newly collected and stored biospecimens that are part of ECHO in accordance with the requirements of 45 CFR 46 for protection of human research subjects, and the requirements of HIPAA (45 CFR 160 and 164) for the protection of individually identifiable health information, as well as the priorities of the ECHO initiatives, and the principles of good scientific methods.

III. Scope

This policy applies to all ECHO and non-ECHO investigators, including ECHO affiliate investigators, engaged in biospecimen activities and/or who request the use of ECHO biospecimens. The biospecimens that are collected in the IDeA States Pediatric Clinical Trials Network are not governed by this policy. ECHO Program initiatives related to biospecimen utilization are to build on the foundation set forth in this policy.

IV. Definitions

Item	Description
Biospecimen	Material taken from the human body (e.g., blood, urine, tissue).
CHEAR	Children's Health Exposure Analysis Resource
CC	Coordinating Center
DAC	Data Analysis Center
ECHO affiliate investigator	Any investigator who is sponsored by an ECHO investigator, and located at the sponsoring investigator's institution
ECHO Cohort Awardee	The 31 ECHO Cohort Awardees, comprising approximately

	70 constituent cohorts.
ECHO investigator	Any member of the ECHO Consortium who is supported by an ECHO grant, subcontract, or consultancy. Support is reflected by the designation as a PI, MPI or Co-I on the grant or subsequent progress reports.
Non-ECHO investigator	Any researcher who is not an ECHO investigator or ECHO affiliate investigator.
ECHO Single IRB	One Institutional Review Board (IRB) of record for multi-site studies that are conducting the same protocol to help streamline the IRB review process by eliminating the unnecessary repetition of those reviews across sites. The ECHO single IRB is Western Institutional Review Board (WIRB) – Copernicus.
ECHO-wide Cohort Data Collection Protocol (EWCP)	The protocol that specifies what data and biospecimens cohorts should collect (new) and share (both existing and new) across the life course from preconception through adolescence. This protocol facilitates the creation of ECHO-wide Cohort data platform.
ECHO-wide Cohort Analysis	An analysis that involves at least 2 Cohort Awardees.
Essential Biospecimen	Biospecimen that ECHO requires cohorts to collect under the ECHO-wide Cohort Data Collection Protocol. Collection and sharing of essential data elements (including biospecimens) is required for participation in ECHO.
Biorepository	Location of stored TYPE C biospecimens (defined below) available for analyses. Fisher BioServices serves as the vendor for the ECHO biorepository.
PII	Personally identifiable information.
Recommended Biospecimen	Biospecimens that ECHO strongly encourages, but does not require, cohorts to collect. If a cohort collects a data element that appears in the ECHO-wide Cohort Data Collection Protocol as recommended, they are expected to share those data with the ECHO-wide Cohort.

V. Policy

A. Types of ECHO Biospecimens

The term ECHO biospecimens refers to biologic samples used for research purposes by

ECHO. The following typology distinguishes, as necessary, among ECHO biospecimens types:

TYPE A: Biospecimens collected through non-ECHO Program funding. These biospecimens are not stored in the ECHO Biorepository. However, metadata for these biospecimens may be available at the ECHO Data Analysis Center (DAC). Additional metadata may be available from the investigators who collected the original biospecimens.

TYPE B: Biospecimens collected through ECHO Program funding to address ECHO cohort-specific aims or other projects, such as Opportunities and Infrastructure Fund (OIF) projects. These biospecimens are not stored in the ECHO Biorepository unless converted to TYPE C biospecimens. The metadata for converted biospecimens will be available at the ECHO DAC.

TYPE C: Biospecimens included in, and collected under, the EWCP. These are stored in the ECHO Biorepository. TYPE C specimens are designated as "Essential" or "Recommended" for a particular subject at a particular life stage.

It is possible for a particular biospecimen (e.g., maternal prenatal plasma) to fall into multiple categories, TYPE A, B, and/or C, for a given cohort.

B. Sharing of Biospecimens that are Collected Prior to the Launch of the ECHO- wide Cohort Data Collection Protocol

TYPE A Biospecimens

The National Institute of Health (NIH) ECHO Program Office expects that the ECHO Cohort Awardees share TYPE A biospecimens that were collected prior to the launch of the EWCP that were deemed essential or recommended (based on biospecimen type, subject, and life stage at collection) in the EWCP. These TYPE A biospecimens should be contributed towards two or more ECHO-wide cohort analyses approved during the 36-month period comprising the second UG3 year and the first and second UH3 years. ECHO Cohort Awardees that elect to contribute Type A biospecimens towards an OIF analysis that has two or more ECHO Awardees will satisfy the Type A sharing metric. This metric does not apply to ECHO affiliate investigators or non-ECHO investigators.

ECHO will initially focus on soliciting and approving TYPE A biospecimens so that ECHO Cohort Awardees will know the universe of potential analyses involving TYPE A specimens in which they can participate.

ECHO Cohort Awardees that do not meet this expectation will provide a rationale to ECHO Program Office at the end of the second UH3 year. Acceptable reasons for not meeting this expectation include:

- The Awardee did not previously collect *any* TYPE A biospecimen deemed *essential* or *recommended* under the EWCP.
- The *essential* or *recommended* TYPE A biospecimen types previously collected bythe

Awardee were not proposed for use in approved Analysis Proposals.

- The *essential* or *recommended* TYPE A biospecimen previously collected by the Awardee has all been used in, or committed for use in, other funded analyses, including ECHO cohort-specific aims.
- Only a single uncommitted aliquot with quantity less than two times the volume required for an ECHO-wide analysis is available.
- Previously collected biospecimens do not meet collection, processing, and storage procedures required for an ECHO-wide analysis.
- Local Institutional Review Board (IRB), other institutions, or other essential partners whose approval is required to permit sharing, would not grant such approval (for example, if the consents signed by the participants do not allow for broad sharing of specimens or are restricted to certain types of investigations).

ECHO Cohort Awardees will share TYPE A biospecimens after the ECHO Steering Committee approves an Analysis Proposal involving that biospecimen type.

TYPE B Biospecimens

The NIH ECHO Program Office expects that the ECHO Cohort Awardees convert TYPE B biospecimens, that were collected prior to the launch of the EWCP that were deemed *essential* or *recommended* (based on biospecimen type, subject, and life stage at collection) in the EWCP, to TYPE C biospecimens and transfer to the ECHO Biorepository, if they meet all of the following conditions:

- There will be biospecimen quantity equal to or exceeding the target amount in an ECHO-wide Cohort analyses remaining after completion of all analyses required to meet ECHO award-specific aims;
- The Award will *not* collect new biospecimens of this type from the same subjects in the same life stage after initiation of the EWCP;
- The biospecimens meet minimum QA/QC requirements around collection, processing, and storage as established by ECHO; and
- Local IRB, other institutions, or other essential partners whose approval is required to permit sharing, grant such approval(s).

This does not apply to ECHO affiliate investigators or non-ECHO investigators.

C. Sharing of Biospecimen that are Collected after Launch of the ECHO-wide Cohort Data Collection Protocol

TYPE A and TYPE B Biospecimens

ECHO Cohort Awardees are not expected to share TYPE A or TYPE B biospecimens that are collected after the launch of the EWCP.

If, after the launch of the EWCP, ECHO Cohort Awardees plan new collection of TYPE A or TYPE B biospecimens that also meet EWCP biospecimen, subject, and life stage criteria for *essential* or *recommended* biospecimens, Awardees are expected to simultaneously conduct TYPE C collection.

ECHO Cohort Awardees collecting new *essential* or *recommended* TYPE C biospecimens for subjects in a particular life stage where this same biospecimen type was previously collected as a TYPE B biospecimen, will not be obligated to share that TYPE B biospecimen (since new TYPE C biospecimen in this same type and life stage will become available for this subject).

If an ECHO Cohort Awardee faces challenges in meeting EWCP obligations for these *essential* or *recommended* TYPE C biospecimens while also fulfilling the scientific obligations of the activity motivating the TYPE A or TYPE B collection, they must contact the NIH Program Office as soon as possible.

TYPE C Biospecimens

The ECHO cohorts must share any *essential* or *recommended* biospecimens collected under the EWCP with the ECHO Biorepository. The biorepository will store and catalog all TYPE C biospecimens (including TYPE B biospecimens that are converted to TYPE C).

The CORE Laboratory Information Management System (LIMS) at the Biorepository is integrated with Bio-Track, the biospecimen management system hosted by the ECHO Data Analysis Center (DAC). Bio-Track provides local tracking of TYPE C biospecimens from the point of collection until shipped to the biorepository in addition to storing all biospecimen data.

D. Approvals Required for Utilization of Biospecimens in Analyses

For any analysis involving a biospecimen, regardless of biospecimen type, all researchers must follow the process for an approved Analysis Proposal. For more details, refer to ECHO Publications Policy.

Appropriate IRB approvals are also required. Local IRB approval is required for TYPE A and TYPE B biospecimens. For TYPE C biospecimens, IRB approvals are required from the local and/or single IRB under the EWCP and consents.

In addition, approval from institutions or other essential partners (e.g., tribal nations) to permit biospecimen sharing will also be required in some instances.

E. Biospecimen Access

TYPE A and B biospecimens to be used in approved ECHO-wide analyses will remain under the control of the local repository. The ECHO Biorepository will hold TYPE C biospecimens, including Type B-converted. CHEAR labs, or an outside laboratory that has been approved

to conduct specific analyses delineated in an approved Analysis Proposal, will have access to the biospecimens. Investigators will not directly access TYPE C biospecimens and cannot use TYPE C biospecimens for cohort-specific analyses or OIF projects.

The ECHO DAC and ECHO investigators will make an integrated decision about the timing of making TYPE C biospecimens available for analysis (possibly different depending on the type of biospecimen in question). The DAC and ECHO investigators will consider the following in determining an appropriate lag time prior to making biospecimens available:

- Biospecimen quality considerations.
- Evidence of selection bias from analyzing biospecimens from cohort participants seen earlier vs. later in a data collection cycle.

All unused biospecimens of sufficient quantity and quality must be returned to the local biorepository (TYPE A and TYPE B) or the ECHO Biorepository (TYPE C) within 4 months of the completion of laboratory analyses.

Biospecimens shipped between Awardee field collection sites, local biorepositories (TYPE A and TYPE B), the ECHO Biorepository (TYPE C), CHEAR labs, and/or other approved analysis laboratories will include appropriate aliquot labels that do not include any PII.

Biospecimens will be transferred between biorepositories and analysis laboratories under Materials Transfer Agreements (MTAs), if necessary.

F. Access to Results from Laboratory Analyses of Biospecimens

For analyses involving data and specimens collected under the EWCP (TYPE C), CHEAR and approved analysis labs provide results through the ECHOPortal. Results are not shared directly with ECHO investigators or any other parties. Once in the ECHOPortal, all aspects of the ECHO Cohort Data Sharing Policy apply to these data. Investigators access these data according to those policies.

When an analysis involves TYPE A and/or TYPE B specimens and existing data, e.g., multi awardee analysis or a OIF project, CHEAR or the approved analysis labs provide results directly to the ECHO investigator. There may be some exceptions when results are sent directly to the DAC e.g. Genome-Wide Association Study results.

G. Disposition of TYPE B Biospecimens

Should an Award no longer be able to store TYPE B biospecimens locally (for example, if ECHO UG3 cooperative agreement supported collection and storage is not continued into the UH3 phase), these biospecimens will be considered for transfer to the ECHO Biorepository as a special collection.

H. Annual Physical Repository Review

At the beginning of each grant year, the Biospecimens Working Group in collaboration

with the DAC, CHEAR, CC, Publications Committee, and the Biorepository, will conduct a review of the biospecimens inventory to ensure optimal and efficient use of TYPE C biospecimens.

The review will consider: 1) analyses of biospecimens completed; 2) analyses approved but not completed; 3) available amounts of various biospecimen types (by visit, participant and cohort); 4) freeze thaw cycles of various biospecimen types; and 5) other aspects of repository operations and biospecimen-based analyses as indicated. This review will provide reference materials and guidance for ECHO in the upcoming year.

I. Resources

The following figures provide guidance related to the allocation of resources for biospecimen transfer:

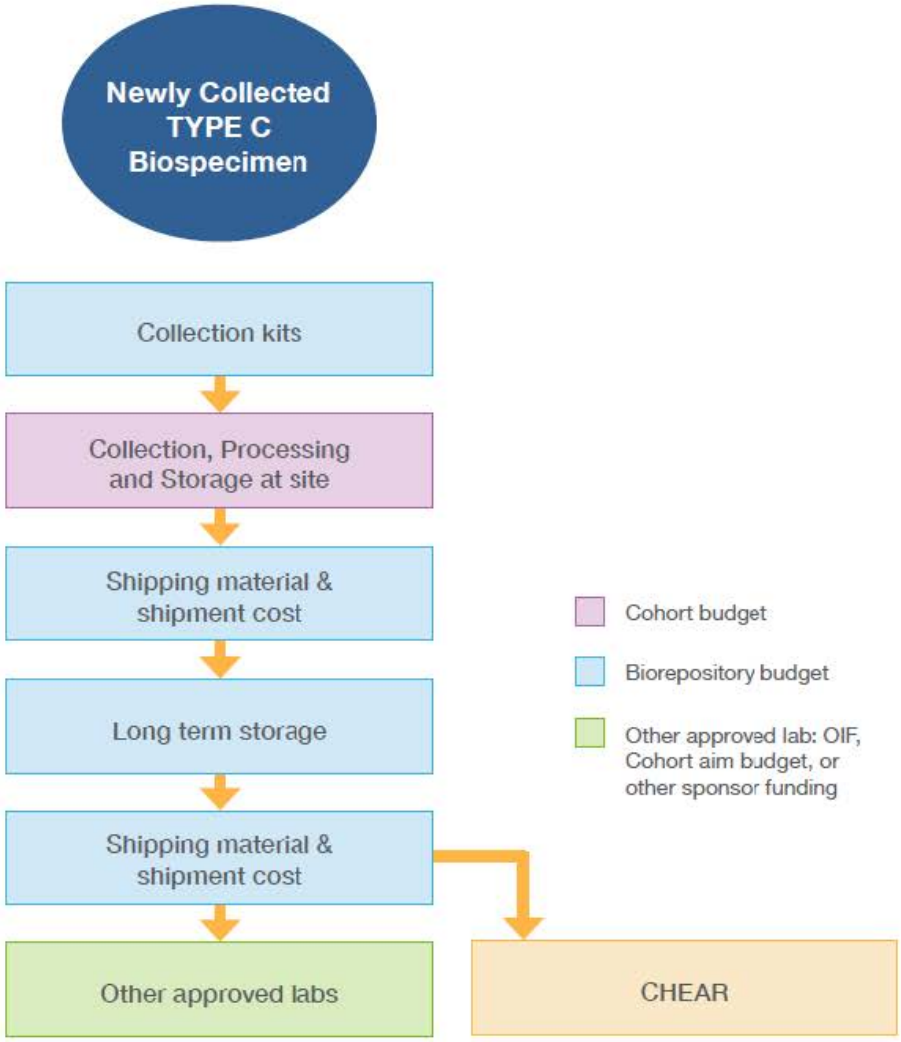

Figure 1: Newly Collected TYPE C Biospecimens

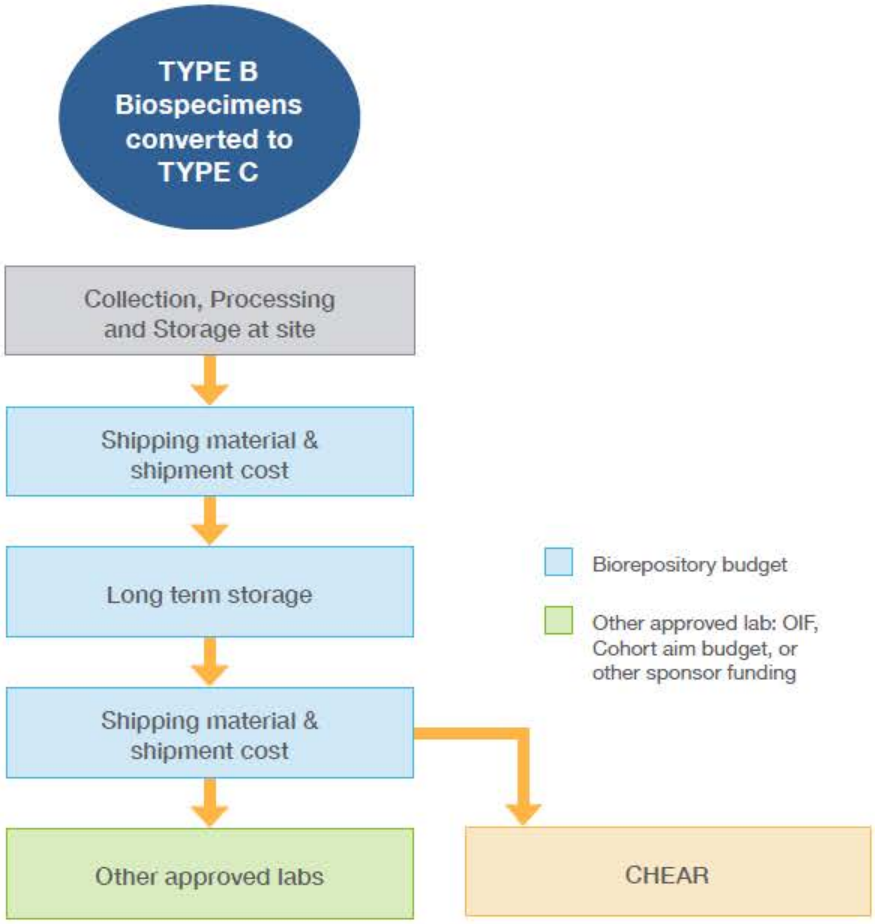

Figure 2: TYPE B Biospecimens converted to TYPE C

VI. Review and Revision

Review of all ECHO Program Manual documents occurs at least every two years; however, more frequent review may be warranted as processes change or major edits are identified.

VII. Supporting Documents

None

VIII. References

A. Data Sharing Policy

B. Publications Policy

C. Collection, Processing and Storage Processes

D. Biospecimen Utilization Processes

IX. Attachments

None

X. History of Change (Since Last Version)

Section Affected	Changes Made
08Nov2017	New document
08Jul2019	Included ECHO affiliates, extended timeframe to share TYPE A specimens towards two approved analysis proposals, removed referenced to existing biospecimen metadatabase, and clarified language throughout the document.

Approval Page

Name/Title	Signature/Date
ECHO Steering Committee	08Nov2017 (v1.0)
ECHO Steering Committee	08Jul2019 (v2.0; via electronic vote)