ECHO Biospecimens Collection, Processing & Storage Policy

I. Introduction

Under direction from the ECHO Steering Committee, this policy facilitates the standardization of and provide quality control for collection, processing, and storage of biospecimens collected by all ECHO Cohorts. The intent is to ensure that the cohorts carry out processes in a consistent manner across all research sites.

To accomplish these goals, this Policy as well as a related process document will provide the detailed procedures for the collection, processing, and storage of ECHO biospecimens. The Biospecimen Utilization Policy directs the Investigator's utilization and management of ECHO Biospecimens and should be used in tandem with this policy. Cohorts are expected to adhere to the Biospecimen Utilization Policy and Collection, Processing and Storage policy when collecting, processing and storing TYPE C and/or TYPE A and B biospecimens; however, biospecimens with additional ownership claims may have modifications in collection, processing and storage procedures and additional steps in approval for use of these samples in ECHO-wide cohort analyses.

II. Purpose

This document provides the overarching policies for biospecimens collected as part of the ECHO Program. Furthermore, it defines the framework for robust and transparent collection, processing and storage process documents, including data management procedures that enable reproducible research. Lastly, it identifies and delineates collaborations that support procedures related to collection, processing, and storage.

III. Scope

This policy applies to all ECHO Program components and pediatric cohorts that facilitate and participate in biospecimen activities related to collection, processing and storage. All ECHO Program initiatives related to biospecimens collection, processing and storage are to build on the foundation set forth in this policy.

IV. Definitions

Item	Description
AO	Analyte-optimized process optimization tier
CHEAR	Children's Health Exposure Analysis Resource
E	Enhanced process optimization tier
MA	Minimum Acceptable process optimization tier

Physical Biorepository	Collection of physically co-located ECHO TYPE C biospecimens available for analyses.

V. Policy

A. Biospecimens Types

The Biospecimens Working Group identified three biospecimens types as part of the ECHO Program and full definitions are provided in the Biospecimen Utilization Policy. Figure 1 outlines the 3 main sample types (TYPE A, B, and C). TYPE C biospecimens can be further subdivided into those that are collected to address specific research questions and have known analytic targets (TYPE C-targeted) and those that are collected without specific analytic targets to be stored and used for future research (TYPE C-general purpose).

B. Biospecimen Standards

The ECHO cohort sites each have varying resources and capacities for specimen collection. In order to optimize the potential for the collection of ECHO biospecimens and maximize flexibility for future use, three levels of rigor in collection, processing and storage are outlined below.

Minimum Acceptable (MA): Biospecimens meeting the MA criteria will be acceptable for validated measurements of some, but not all analytes. (e.g., total white blood cell DNA from buffy coat; biospecimens collected in containers not prescreened for specific chemical contaminants).

Enhanced (E): Biospecimens meeting the E criteria must meet 'Minimum Acceptable' criteria and also meet additional criteria that allow for specific analyses or use of designated analytic platforms that require more specialized biospecimens handling for validated measurement. (e.g., DNA from buffy coat PLUS DNA collected in ficoll tubes for mononuclear cells; blood or serum collected in prescreened tubes for trace element analysis).

Analyte-optimized (AO): Biospecimens that meet the AO criteria allow for use of ECHO biospecimens for validated measurement of specific analytes that require specialized collection and/or storage procedures. (e.g., DNA from buffy coat PLUS DNA cell-sorted blood; blood collected in PAXgene tube for RNA; plasma from blood collected in P100 tubes for proteomics).

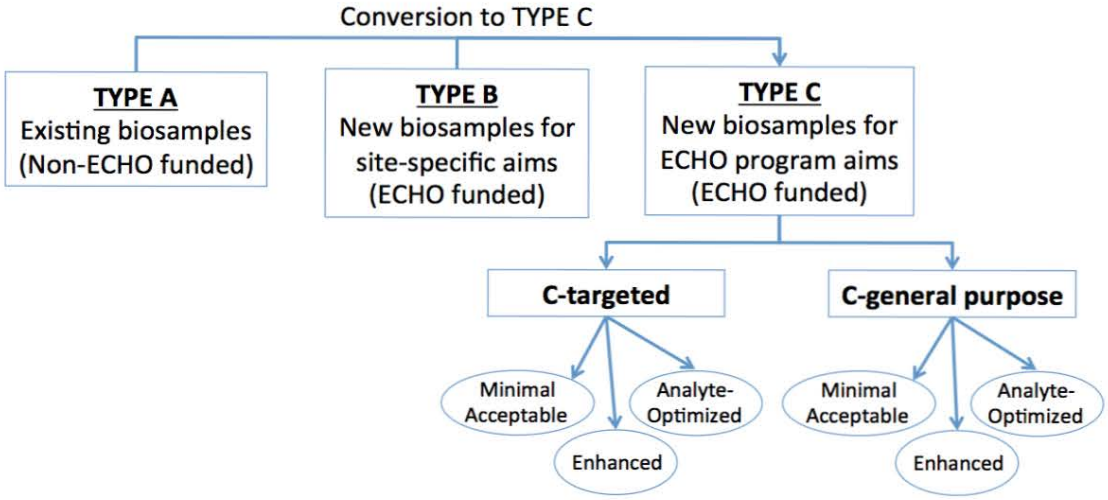

Figure 1 Integration between biospecimens type and process optimization

Supporting process documents will outline a tiered set of collection, processing and storage criteria for each biospecimen type that will allow for the collection of biospecimens for analysis of specialized targets that are defined as AO (e.g. RNA, which needs inhibitors to maintain biospecimens stability). These documents will also define processes that will maximize the likelihood of adherence to collection procedures aimed at safeguarding the valid measurement of an array of target analytes (MA and E biospecimens).

C. Participant Sensitivities

Information in this section is relevant to collection, processing and storage of biospecimens across all ECHO protocols. Collection procedures will be sensitive to 1) the amount of the biospecimens that is acceptable for participants to donate at different life stages; 2) cultural considerations of study participants; and 3) minimizing invasive procedures.

1. The quantity of certain types of biospecimens collected may be limited for any number of reasons (e.g., IRB approvals, feasibility, and willingness of participant). Furthermore, the maximum quantity collectable from a participant may vary across life stages. Therefore, specific collection processes and related initiatives will reflect safe and acceptable biospecimens volumes for the participants in consideration with their life stage. Additionally, the cohort principal investigator must use best judgment in determining whether the amounts required to be collected is excessive given the participant's health history and status at the time of collection.
2. Some biospecimens (e.g., hair, nails, and vaginal swabs) may not have maximal collection limits, but investigators must take care to approach collection in a culturally acceptable manner. Similarly, cultural practices may affect a cohort's willingness to

contribute a particular biospecimen (e.g., cord blood, placenta tissue). While contribution of biospecimens is always voluntary, the ECHO investigators recognize the importance of consideration of cultural factors when creating biospecimen processes. The Collection, Processing and Storage Process document will include information on cultural factors and considerations for specific specimen types.

3. When possible, processes will prioritize non-invasive biospecimens over invasively collected biospecimens and will develop procedures to minimize the number of invasive episodes per participant.

D. Biospecimens Quality

The ECHO cohort sites are to implement specific quality control procedures that minimize the likelihood of biospecimen loss and contamination during handling. These procedures will pertain to all ECHO cohort sites collecting and processing biospecimens and to TYPE C biospecimens stored in the Physical Biorepository.

In addition to the preservation of biological components in the collected biospecimens, it is important to ensure that measurement of environmental pollutants present in the biological biospecimens is not confounded by contaminants introduced by the containers or tools used for biospecimen collection. Prescreening of these materials may be necessary depending on the analyte of interest.

E. Future Analyses

The ECHO Program components and cohorts will collaboratively prioritize types of biospecimens ECHO cohorts sites will collect based on the scientific research questions. Specific biospecimen collection, processing and storage procedures must be implemented to ensure that biospecimens are collected in a manner that will safeguard the valid measurement of biomarkers required to address these high priority research questions (TYPE C-targeted). Associated procedures will allow for the analysis of a wide variety of target analytes, with the goal of enabling future analyses (TYPE C-general purpose).

F. Collaborations

Biorepository Vendor

The Biorepository vendor plays a critical role in the development of biospecimen collection, processing and storage procedures. The following areas will be addressed via this collaboration that fall under the jurisdiction of the Biorepository vendor:

1. Ensure that there is robust and transparent documentation for biospecimens and associated metadata stored and maintained by the Biorepository.

2. Develop a plan for the preparation of multiple replicate biospecimens that can be stored at two or more locations.
3. Maintain biospecimen integrity during long-term storage and develop cataloging, naming, protocol vetting and retrieval systems for biospecimen recovery after long-term storage.
4. Develop procedures so newly collected biospecimens will be aliquoted and stored directly into long-term storage tubes (as far as possible) to minimize biospecimen loss and freeze thaw cycles.
5. Consider the types of tubes used, taking into account possible target analytes to avoid cross-contamination. The Biorepository vendor will provide sample collection kits to cohort sites, which will minimize cross-contamination and facilitate background correction.
6. Distribute coded labels or a point of collection label printing system so that it is available at time of initial biospecimen collection to minimize errors.

NIEHS Children's Health Exposure Analysis Resource (CHEAR)

A CHEAR representative actively participates in specific activities related to biospecimen analysis and helps to identify TYPE C biospecimens that will be used for future analysis that are thus far unspecified (TYPE C-general purpose).

VI. Review and Revision

All ECHO Program Manual documents, including the collection, processing and storage policy document and process 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. As there are many decisions currently under consideration that may have implication for both the CPS Policy and Processes documents, the Biospecimen WG leaders plan to re-evaluate these policies every 6-months following their approval.

VII. Supporting Documents

A. Collection, Processing and Storage Process Documents

The Collection, Processing and Storage Process Documents will specify the requirement for detailed documentation of each aspect of sample handling including collection, processing and storage. The CPS Subgroup will move forward with the development of these Process Documents with the expectation that revisions may be necessary as the ECHO program develops.

VIII. References

A. Biospecimen Utilization Policy

IX. Attachments

None

X. History of Change (Since Last Version)

Section Affected	Changes Made

Approval Page

Name/Title	Signature/Date
ECHO Steering Committee	November 8, 2017