SHIPMENT OF CLINICAL SPECIMENS TO THE IMPAACT SPECIMEN REPOSITORY

Standard Operating Procedure

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DOCUMENT CONTROL

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I. Purpose

To describe the requirements and procedures for shipment of clinical specimens from both domestic and international NIAID-funded sites to the IMPAACT Specimen Repository at Fisher Bioservices (Fisher).

II. Definitions

ACTG – AIDS Clinical Trials Group
ACTN – AIDS Clinical Trials Network
BRI – Biomedical Research Institute
CLS – Central Laboratory Specialist
CD – Compact Disc
CPS – Cryopreservation Solution
DBS – Dried Blood Spots
DMC – Data Management Center
FAB – Finance and Budget
IATA – International Air Transport Association
LDMS - Laboratory Data Management System
LN2 – Liquid Nitrogen
MIIRF – MTA Institution Request Form
MOP – Manual of Procedures
MTA – Material Transfer Agreement
MVE – MVE Biological Systems, manufacturer of cryoshippers
NIAID – National Institute of Allergy and Infectious Diseases
NICHD – Eunice Kennedy Shriver National Institute of Child Health and Human Development

PBMC – Peripheral Blood Mononuclear Cell
RLMP – Retrovirology Laboratory Management Program
SAR – Subcontract Action Request

III. Specimen Repository Facility

Fisher Bioservices

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301-340-1620

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LDMS # 243

IV. Applicability

- These procedures for specimen shipment and storage apply to specimens collected at clinical sites affiliated with the Eunice Kennedy Shriver National Institute for Child Health and Human Development (NICHD), National Institutes of Health (NIH).

- Clinical sites and other research networks participating in IMPAACT clinical research studies that are affiliated with other NIH Institutes, such as the National Institute of Allergies and Infectious Disease (NIAID), should follow their respective repository instructions.

V. Requirements for Short-term and Long-term Specimen Storage

- Unless otherwise specified in the protocol, specimen storage is of two types: (i) short-term storage with specimen disbursement to testing laboratories at protocol-specified times and (ii) long-term archival storage.

- Short-term storage at the Repository applies to protocol specimens that will be batch tested more than 6 months after collection.
    - Specimens designated for "real-time" testing should be shipped directly to the testing laboratory.
    - Specimens that are not designated for "real-time" testing but will be tested within 6 months of collection should be held at the primary collection site and shipped to the testing laboratory at a time specified by the protocol.

- Batch testing of specimens that will occur more than 6 months after collection should be shipped to the Fisher Repository when there is a full box or every six months unless otherwise indicated in the protocol.

- Long-term archival storage at the Fisher Repository refers to storage of specimens that are designated for future studies as defined in the protocol and the NICHD repository consent. These specimens can remain in storage for an indefinite period of time.

- The specimen type (primary, additive, derivative and sub-additive/derivative) and number of samples that are to be shipped to the Fisher Repository on a regular basis are specified in the Appendix section of each protocol and/or in the Laboratory Processing Chart.

VI. Shipping Schedules

- Shipments should be made Monday through Wednesday. Shipments should be sent via overnight courier. No shipments should be made within two days of a holiday. The Fisher Repository is closed on weekends and many federal holidays and will be unable to receive the shipments. Holiday closures include: New Years Day, Martin Luther King Day, President's Day, Memorial Day, July 4th, Labor Day, Thanksgiving Day, the day after Thanksgiving, and Christmas Day.

- Domestic and International Labs requiring Dry Nitrogen Shippers: At least one week prior to the site's shipping week, the Fisher Repository will ship shipping containers from the Fisher Repository according to the scheduled established by the Laboratory Specialist. **NOTE: LN_2 dry shippers are available from Fisher Repository but due to limited availability, containers will be rotated between laboratories on the NICHD list.**

- International sites will ship to the Repository as outlined in specific protocols. This may or may not involve routine shipments to the Fisher Repository, but other guidelines for shipments do apply.

- The sites are required to use approved shipping containers to reduce improper packaging problems. All the components of the shipping containers must be used in order to comply with International Air Transportation Association (IATA) regulations. No substitution of any components from other containers is allowed.

- All IATA Dangerous Goods regulations must be followed when packing, labeling and shipping specimens. **Study and laboratory personnel involved with packaging and transporting specimens must receive adequate and appropriate training to ensure compliance to guidelines and regulations. Refer to the "ACTN Shipping Guidelines" document on the IMPAACT web site https://member.impaactgroup.org/cms/folder/7696**

- The shipping site must either email (maria.wolff@thermofisher.com and fbs.gbo@thermofisher.com) or fax a notification prior to shipping using the "Specimen Shipment Notice" found on the IMPAACT web site https://impaactgroup.org/

VII. Storage Box and Shipping Requirements

- Laboratories must send full boxes to the Fisher Repository to avoid unnecessary specimen manipulation associated with repackaging and consolidating boxes at the Repository.
    - For IMPAACT, storage boxes may be filled with specimens from multiple protocols to meet the full box requirement.
    - For sites that have a low number of study subjects and are unable to fill a storage box, less frequent shipments to the Fisher Repository are allowed. These specimens can be held at the site/laboratory for up to 6 months. After 6 months, the specimens should be sent to the Fisher Repository. Please separate the cryopreservation solution (CPS) pellets from the serum, plasma, or urine.
    - Refer to the Specimen shipping guidelines and LN_2 shipping instructions on the website: http://www.hanc.info/labs/labresources/Pages/informationActgImpaactLabs.aspx
    - Before shipping any specimens to Fisher Repository in LN2, please refer to Filling and Packing Instructions for MVE Cryoshippers available at the end of this SOP.

Note: Multiple boxes are now allowed in single shipment batches, meaning, one shipping manifest and a shipment package can contain more than one freezer (specimen) box. Each specimen box is not required to have its own manifest. Manifests from multiple batches in the same shipment can be combined and sent in the shipment package.

- 2-inch fiberboard storage boxes are to be used for shipments to the Repository. The 9x9 or the 8x8 box arrays are recommended for the 2.0 mL Nunc, Wheaton or Corning tubes; the 10x10 box array should only be used for 1.8 mL Sarstedt brand tubes.
- 2-inch fiberboard boxes are also to be used for shipping Dried Blood Spots (DBS) for 1077HS study to the Repository. Refer to the 1077HS protocol Manual of Procedures (MOP) for specific storage and shipping instructions.
- 3-inch fiberboard boxes may be used for shipping to the Repository if the protocol mandates larger volume storage. Only 3.6 mL cryovials should be used with 3-inch fiberboard boxes.
- Boxes of mixed protocol specimens designated for storage in -70°C freezers (serum, plasma, pellets, etc.) can be shipped on dry ice in the same shipping container. Please keep the pellets that will be stored in liquid nitrogen separate from the other samples.

- **Effective 04 November 2011, boxes of cryopreserved viable peripheral blood mononuclear cells (PBMC) intended for storage in liquid nitrogen must be shipped in IATA complaint LN_2 cryoshippers (also known as dry shippers).**

- For cryopreserved PBMC, liquid nitrogen rated fiberboard storage boxes should be used. This will allow for the direct placement of the shipment into liquid nitrogen at the Repository. These boxes should also be vented with drainage holes. **Do not send plastic storage boxes for liquid nitrogen or -70°C storage.**

- **All IATA Dangerous Goods regulations must be followed when packing, labeling, and shipping specimens. All domestic and international regulations require that individuals who pack and ship biological specimens must be trained and certified in Dangerous Goods Shipping.**

VIII. LDMS Labeling Requirements

- A Laboratory Data Management System (LDMS) electronic shipping file stored on a diskette or CD must accompany all specimen shipments to the Repository at Fisher. **Sites may send shipping files via email, which is preferred, as diskettes and CDs are sometimes damaged.**

- Specimens must be uniformly labeled according to an LDMS-specified format, which will require a computer-generated label containing specific identifiers.

- All IMPAACT specimens stored after 01 October 2008 must be labeled with a LDMS generated barcode. Specimens collected before that date can have printed or hand written labels that include the following elements:

    - PID
    - Global Specimen ID (only for specimen dates after September 1, 2005: not required for hand-written specimens)
    - Protocol
    - Specimen Date
    - Primary/Additive/Derivative/Sub-additive
    - Specimen Time (24 hour clock)

- All IMPAACT sites and laboratories must comply with the electronic LDMS inventory and labeling protocol. However, under the following circumstances, legible hand-labeled specimens will be accepted provided that the specimens are accompanied by an LDMS electronic shipping file **(NOTE: these are unusual circumstances considered the exception, not the rule):**

- Specimens that were legibly hand-labeled prior to and during the transition period from the Retrovirology Laboratory Management Program (RLMP) to the LDMS;

- Printer or computer malfunction (note: ideally, re-labeling with printed labels should occur **prior to shipping to the Repository**);

- Specialized processing constraints that must be accomplished before access to an electronic label can be attained (e.g., PK or metabolic specimens).

Note: Comments must be added to the LDMS regarding re-labeling. These comments are acceptable for all tube discrepancies, except PIDs and Global SpecIDs. The IDs must match the LDMS/shipping manifest otherwise the testing labs will not accept them.

- Care should be taken that the specimen shipments comply with the labeling requirements and include the appropriate LDMS-generated documents/files, including accurate box maps. Fisher Repository personnel performs a quality check of 100% of the specimens received, and any sites will be notified of discrepancies. **NOTE: International shipments will be held to the same standard as the domestic shipments. Reconciliation of problem shipments will be required.**
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- All IMPAACT shipments to the Repository must include:
  - LDMS-generated shipping manifest
  - LDMS-generated box map
  - LDMS shipping electronic file stored on a diskette or CD

- All specimen-processing sites **must use the LDMS** as a prerequisite for shipping specimens to the Fisher Repository. Those subunits without the LDMS should either acquire the LDMS or arrange with their main clinical or laboratory site to electronically label and enter specimens in to the LDMS site database before shipment to the Fisher Repository.

- Both the shipping file and storage boxes must be labeled with the batch number and laboratory or clinic site number. Multiple boxes can be put into the same shipping batch and in a single file on a diskette or CD. A shipping file on a diskette or CD must be included with each shipment.

- For specimen disbursement from the Fisher Repository to the testing site, each shipment from the Fisher Repository will be accompanied by a shipment (inventory) file, manifest and box map. The file will be used to import the shipped inventory into the receiving (testing) site's LDMS or other electronic inventory system, where appropriate, for either commercial or non-IMPAACT testing laboratories.

IX. Evaluation of Specimen Shipments to the Fisher Repository

- All specimen shipments to the Fisher Repository from the clinical and laboratory sites will be evaluated for compliance with proper specimen labeling, packaging, and shipping.
- The DMC will track the number and type of specimens to be sent to the Fisher Repository by each site/laboratory based on LDMS data exports from the Fisher Repository.

X. Prioritization of Specimen Shipments

- Information on the current list of approved shipments to the Fisher Repository can be found in the individual protocol LPC on the IMPAACT website.

XI. Transfer of Specimens to Testing Laboratories

- To have specimens transferred from the Fisher Repository to a testing laboratory the protocol team **must** submit the specimen request form found on the DMC web page. Alternatively, the team can ask the Data Manager or **Laboratory Data Coordinator** for the study to submit the specimen request on their behalf.
- The DMC will generate a report of specimens to be shipped by the Fisher Repository to the testing laboratory. The Fisher Repository will locate the specimens and ship them to the testing laboratory with an electronic shipping file and shipping manifest. At the testing laboratory, the information will be imported into the LDMS and the specimens tested. At the discretion of the protocol team, any unused specimens may be returned to the Fisher Repository for archiving, stored on site, or discarded.

Any questions concerning these procedures can be addressed to the Westat Laboratory Specialist at franceswhalen@westat.com.

Filling and Packing Instructions for Cryoshipper

Note: Begin this procedure at least 24 hours prior to the planned time of shipping.

Filling:

1. Remove the secondary container when filling liquid nitrogen into the shipper.
2. Fill the unit to the bottom of the neck and allow the liquid nitrogen to absorb.
3. Four hours later, repeat with another fill to the same level.
4. Four hours later, (i.e. 8 hours from initial fill) repeat with another fill.
5. At least 16 hours later (i.e. 24 hours after initial fill) and just prior to shipment, pour out the excess liquid nitrogen. Do not pour out the liquid nitrogen until you are ready to load the shipper with the specimen boxes/vials you plan to ship. There should be no liquid left inside the shipping container.
6. To insure that the vapor shipper has absorbed the full capacity of liquid, it is necessary to weigh the shipper. The empty weight of the unit without the plastic outer container and inner secondary container is 30 lbs**. (Please weigh your specific containers prior to the filling steps.)** The full weight should be about 47-50 lbs. This will allow the shipper to hold maximum number of days in the vapor phase. If the full weight is less than 47 lbs. it may be necessary to repeat the process.

Packing:

7. Pre-cool the secondary container in liquid nitrogen vapor phase or -70 C mechanical freezers before placing boxes inside.
8. Place one rubber band around each specimen box.
9. Place one absorbent sheet around each specimen box and secure with a second rubber band.
10. Place the boxes (maximum of 4 – 81 tube containers) inside the secondary container. Do not force boxes in to metal container. Please contact Fisher for further instructions if boxes are too big. Do not put dry ice or liquid nitrogen inside the secondary container. Do not use plastic biohazard bag or envelope. They are not required.
11. Seal the lid with all six screws using the wrench provided. Do not over tighten.
12. Place the secondary container inside the shipper and place lid on shipper. Secure lid with the twist tie.
13. Place the shipping manifest and diskette inside the plastic bag and tape to the metal lid.
14. Buckle the outer plastic shipping container and place tape over the buckles.

SHIPMENT OF CLINICAL SPECIMENS TO THE IMPAACT SPECIMEN REPOSITORY

Packing and Shipping LN2 Specimens to the Fisher Repository for NICHD IMPAACT Specimens

These specimens are now classified as BIOLOGICAL SUBSTANCE, CATEGORY B, per the IATA Dangerous Goods Regulations.

A Cryoshipper will be sent to your facility every six months to accommodate the required semi-annual shipment of viable PBMCs. The IMPAACT PNL and the ThermoFisher Repository will coordinate the schedule for these shipments.

Shipments must be ready at least two hours prior to your close of business for pickup.

1. Generate a computer printout of the shipping manifest and box map. This manifest and the shipping diskette are to be enclosed with the shipment.
2. Email Fisher that the shipment has been prepared and the day you will be shipping. Contact Maria Wolff and Susan Meslovich at Fisher to let the repository know you are shipping the container. susan.meslovich@thermofisher.com maria.wolff@thermofisher.com
3. Please refer to the instructions for charging and packing the CryoShipper. Place 2 rubber bands and 1 absorbent sheet around each specimen box.
4. Enclose the manifest and diskette on top of the metal lid.
5. Affix the labels to shipping container.
6. Fill in the total weight on the shipping airbill
7. Place the completed airbill on top of the shippers
8. A dangerous good form is not required.
9. These shipments can only be shipped on Monday, Tuesday, and Wednesday. Also please note the repository follows the Federal Government holiday schedule. Do not send a shipment that is due to arrive on a Federal holiday.