National Institute of Neurological Disorders and Stroke Biorepository:

**BioS**pecimen **E**xchange for **N**eurological **D**isorders, **BioSEND**

# Biospecimen Collection, Processing, and Shipment Manual for EpiBioS4Rx Study

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## 1.0 PURPOSE

The purpose of this manual is to provide collection site staff (PIs, study coordinators, and the sample collection and processing teams) at various study sites with instructions for collection and submission of biological samples. It includes instructions for biospecimen submission to the BioSpecimen Exchange for Neurological Disorders (BioSEND) located at Indiana University.

This manual includes instructions for the collection, processing, aliquoting and shipping of the following samples:

- PAXgene® (for RNA extraction)
- Plasma
- Buffy Coat (for DNA extraction)

These procedures are relevant to all study personnel responsible for processing blood specimens to be submitted to BioSEND.

## 2.0 ABBREVIATIONS

| | |
|---|---|
| BioSEND | BioSpecimen Exchange for Neurological Disorders |
| EDTA | Ethylene Diamine Tetra-acetic Acid |
| IATA | International Air Transport Association |
| RCF | Relative Centrifugal Force |
| RPM | Revolutions Per Minute |

# 3.0 BioSEND Information

## 3.1 BioSEND Contacts

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**Claire Wegel, Project Manager**
Phone: 317-278-6158
Email: cwegel@iu.edu

**General BioSEND Contact Information**
Fax: 317-278-1100
Email: biosend@iu.edu
Website: www.BioSEND.org

**Sample Shipment Mailing Address**
BioSEND
Indiana University School of Medicine
351 W. 10th Street, TK-217
Indianapolis, IN 46202-5188

## 3.2 Hours of Operation

Indiana University business hours are from 8 AM to 5 PM Eastern Time, Monday through Friday.

**Frozen samples must be shipped Monday- Wednesday only.**

For packaging and shipment details, please refer to Appendix K (Frozen Shipping Instructions).

Check the weather reports and the shipping courier website to make sure impending weather events (blizzards, hurricanes, etc.) will not impact the shipping or delivery of the samples. Couriers often report anticipated weather delays on their websites.

### 3.3 Holiday Schedules

- Please note that courier services may observe a different set of holidays. Please be sure to verify shipping dates with your courier prior to any holiday.
- **Weekend/holiday deliveries will not be accepted.**

### 3.4 Holiday Observations

| Date | Holiday |
|---|---|
| January 1 | New Year's Day |
| 3rd Monday in January | Martin Luther King, Jr Day |
| 4th Monday in May | Memorial Day |
| July 4 | Independence Day (observed) |
| 1st Monday in September | Labor Day |
| 4th Thursday in November | Thanksgiving |
| 4th Friday in November | Friday after Thanksgiving |
| December 25 | Christmas Day |

Please note that between December 24th and January 2nd (or the first business day after New Year's Day) Indiana University will be open Monday through Friday for essential operations **ONLY** and will re-open for normal operations on January 2nd. If at all possible, biological specimens for submission to Indiana University should **NOT** be collected and shipped to Indiana University between December 24th and January 2nd. Should it be necessary to ship blood samples for DNA extraction to Indiana University during this period, please contact the Indiana University staff before December 24th by e-mailing biosend@iu.edu, so that arrangements can be made to have staff available to process incoming samples. Frozen specimens collected during this period should be held at your site to ship after the first business day in January.

**Please see https://www.biosend.org/holiday_closures.html for additional information.**

## 4.0 BioSEND Sample Requirements

NINDS approves each study for a specific biospecimen collection protocol. Studies and study sites should make every effort to meet their approved biospecimen collection requirements. The expected number of samples from each site that should be returned to BioSEND are listed in sections 4.1

## 4.1 Protocol Schedule for Biospecimen Submission to BioSEND - EpiBioS4Rx

| Visit (month) | D1 | D3 | D5 | D15 | D30 | D90 | D180 |
|---|---|---|---|---|---|---|---|
| | | | | | | | |
| Whole blood for RNA (PAXGene® tube, 2.5ml) | - | - | 2 | 2 | - | - | - |
| Plasma aliquots, 250ul | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Buffy Coat | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

## 5.0 SPECIMEN COLLECTION KITS, SHIPPING KITS AND SUPPLIES

Research specimen collection kits as well as clinical lab supplies (except dry ice and equipment listed in Section 5.4) will be provided by BioSEND. These materials include blood tubes, boxes for plasma and buffy coat aliquots, as well as partially completed shipping labels to send materials to BioSEND. Barcoded kit labels, collection tube labels, and aliquot tube labels will all be provided by BioSEND. Collection tube labels and aliquot tube labels will be pre-printed with study information specific to the type of sample being drawn. BioSEND will provide a sufficient number of labels only for those specimens that are to be shipped back to the BioSEND repository (See the Protocol Schedule for Biospecimen Submission to BioSEND for your site in Sections 4.1); any tubes that will remain at the collection site should be labeled accordingly. Ensure that all tubes are properly labeled during processing and at the time of shipment according to Section 6.2.

### 5.1 Kit Supply to Study Sites

Kits for a subject are all inclusive. They contain all supplies necessary to collect from a subject for the duration of the visit protocol.

Each individual site will be responsible for ordering the kit from BioSEND. We advise sites to proactively confirm kits are on hand ahead of study visits.

Within the kit request module, there is a drop down menu to request kits based on the Principal Investigator and site number of that site. Kits and individual items can be ordered as required through the kit request module.

The link to the kit request module is shown below:

- EpiBioS4Rx: http://kits.iu.edu/epibios4rx

Please allow **TWO weeks** for kit orders to be processed and delivered.

## 5.2 Specimen Collection Kit General Contents

Collection kits contain the following (for each subject) as designated per your protocol and/or NINDS resource development agreement. Kits provide the necessary supplies to collect samples from a given subject. Do not replace or supplement any of the tubes or kit components provided with your own supplies unless you have received approval from the NINDS/BioSEND Study team to do so. *Please store all kits at room temperature until use.* Note that "supplemental" kits will be provided should you require additional supplies from those contained in the visit specific kits.

**BioSEND Supplies**

Available upon request from the online kit request module (Section 5.1)

| **General Items** |
|---|
| Ambient shipping kits |
| 25 cell cryobox |
| Cryovial tube (0.5 ml) with clear cap |
| Airway bill envelope |
| Shipping container for dry ice shipment (shipping and Styrofoam® box) |
| Plastic biohazard bag |
| Warning label packet |
| **Blood Collection Items** |
| PAXgene® tube (2.5 ml) |
| Lavender-top EDTA blood collection tube (10 ml) |
| |

We realize there may be instances where additional supplies are needed; therefore, one supplemental kit will be provided with the initial kit shipment for new studies. Replacement supplemental kits can be requested on the kit request website. In addition, individual supplies can be requested as well.

## 5.3 Specimen Collection Kit Contents – EpiBioS4Rx

| **Specimen Collection Supplies** | PAXgene® (2.5ml) | EDTA (10mL) | Cryovial (0.5ml) | Cryovial (2.0ml) | Disposable pipet (1mL) | Frozen Shipping Kit |
|---|---|---|---|---|---|---|
| | | | | | | |
| All kits | 4 | 7 | 50 | 10 | 7 | 1 |

### 5.4 Site Required Equipment

The following materials and equipment are necessary for the processing of specimens at the collection site and are to be **supplied by the local site**:

- Personal Protective Equipment: lab coat, nitrile/latex gloves, safety glasses
- Tourniquets
- Alcohol Prep Pads
- Gauze Pads
- Bandages
- Butterfly needles and hubs
- Microcentrifuge tube rack
- Test tube rack
- Sharps bin and lid

In order to process samples consistently across all projects and ensure the highest quality samples possible, project sites must have access to the following equipment:

- Centrifuge capable of ≥ 1500 rcf (1500 x g) with refrigeration to 4°C
- -80°C Freezer

In order to ship specimens, you must provide:

- Dry ice (approximately 10lbs per shipment for standard shippers, 45lbs for bulk shippers)

## 6.0 SPECIMEN LABELS

Labels must be affixed on all collection and aliquot tubes to ensure unique specimen identity. BioSEND provides labels for all samples being collected and returned to BioSEND. The site is responsible for providing labels for biospecimens that will be retained at the site. **If labels are provided but the sample is not collected, please return the unused labels to BioSEND when the specimens are shipped to BioSEND for permanent storage.**

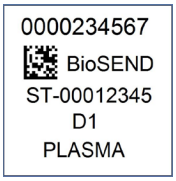
### 6.1 Types of Labels

**Label Type Summary**

1. Case Label
2. Collection and Aliquot Tube Label for Blood

Each kit contains all labels required for the return of biospecimens to BioSEND.


The **Case Labels** do not indicate a specimen type, but are affixed on BioSEND forms and on specific packing materials.

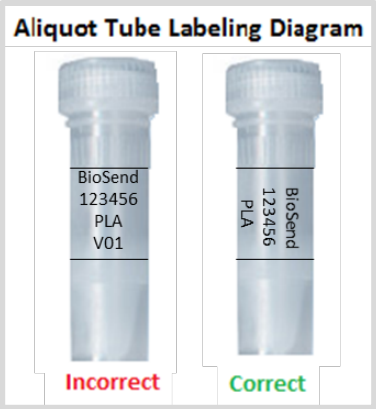



The **Collection and Aliquot Tube Labels for Blood** are placed on all blood collection and aliquot tubes.

### 6.2 Affixing Labels

In order to ensure the label adheres properly and remains on the tube, follow these instructions:

- Place blood collection and aliquot labels on **ALL** collection and aliquot tubes **BEFORE** sample collection, sample processing, or freezing. This will help to ensure the label properly adheres to the tube before exposure to moisture or different temperatures.
- The blood collection and aliquot tube labels contain a 2D barcode on the left hand side of the label. When turned horizontally, the barcode should be closer to the top (cap end) of the tube.
- Place label **horizontally** on the tube (wrapped around sideways if the tube is upright) and **just below the ridges** of the aliquot tubes (see attached labeling diagram).




- Take a moment to ensure the label is **completely affixed** to each tube. It may be helpful to roll the tube between your fingers after applying the label.

# 7.0 SPECIMEN COLLECTION AND PROCESSING PROCEDURES

Consistency in sample collection and processing is essential for biomarker studies. All samples are drawn in the same order and then processed in a uniform fashion. **Please read the instructions before collecting any specimens. Have all your supplies and equipment out and prepared prior to drawing blood.**

## 7.1 Order of Specimen Collection

Blood collection should be performed in the following order:

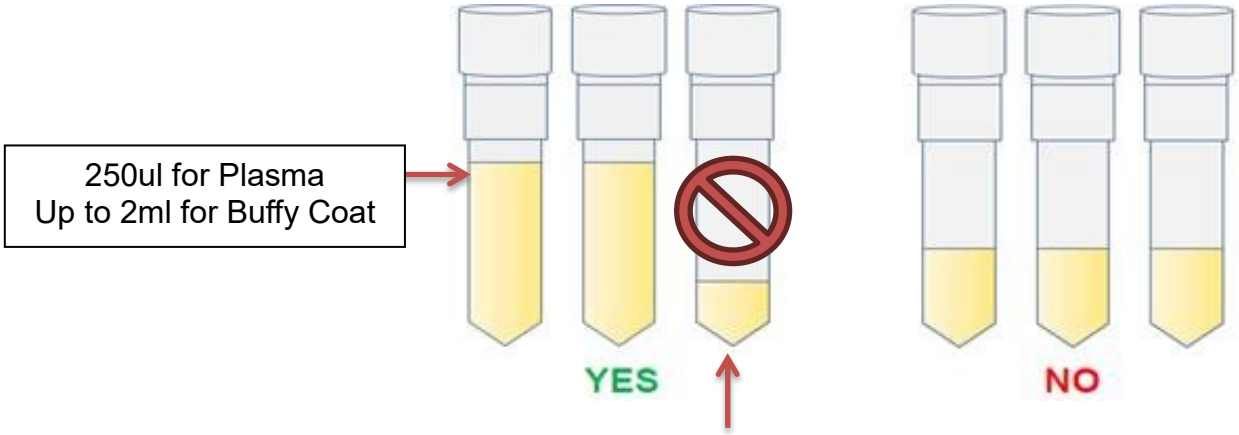
1. PAXgene® tube for RNA
2. EDTA (lavender top) blood collection for plasma and buffy coat

## 7.2 Blood Collection Protocols

1. PAXgene® tube for RNA **(Appendix A)**
2. EDTA (lavender top) blood collection for plasma and buffy coat **(Appendix B)**

### 7.3 Filling Aliquot Tubes (Plasma, Buffy Coat)

In order to ensure that BioSEND receives a sufficient amount of sample for processing and storage, and to avoid cracking of the tubes prior to shipment, each aliquot tube should be filled to the assigned volume (refer to detailed processing instructions for average yield per sample). Over-filled tubes may burst once placed in the freezer, resulting in a loss of that sample. Each site is supplied with sufficient collection tubes to provide the specimen volume described in the Protocol Schedules for Biospecimen Submission (see Section 4). Specimens collected in addition to those described in Section 4 are collected at the site's discretion and are not returned to BioSEND.




**Please note:** It is critical for the integrity of future studies using these samples that study staff **not submit** residual aliquot tubes (anything under instructed volume) to BioSEND.

## 8.0 Packaging and Shipping Instructions

**ALL** study personnel responsible for shipping should be certified in biospecimen shipping. If not available at your University, training and certification is available through the CITI training site (Course titled "Shipping and Transport of Regulated Biological Materials" at https://www.citiprogram.org/).

### 8.1 Biosample shipping form

All sample shipments to BioSEND must include the Biosample shipping form, which can be found in REDCap.

- Emailed to BioSEND@iu.edu at the time the samples are being shipped
- be Included in the shipment with the samples

### 8.2 Shipping Instructions

Frozen Shipments: Reference Appendix K for frozen shipping instructions.

- Frozen PAXgene® Tubes
- Frozen aliquots of plasma
- Frozen Buffy Coat

*****Important Note*****

**Include samples for only one subject per shipping container.**

**For frozen shipments, include no more than two packing envelopes per shipping container in order to have room for a sufficient amount of dry ice to keep samples frozen up to 24 hours.**

### 8.3 Shipping Address

All samples are shipped to the BioSEND laboratory:

BioSEND
Indiana University School of Medicine
351 W. 10th Street. TK-217
Indianapolis, IN 46202-5188

## 9.0 APPENDICES

Appendix A: Whole Blood Collection for Isolation of RNA

Appendix B: Whole Blood Collection for Isolation of Plasma and Buffy Coat

Appendix K: Frozen Shipping Instructions

Appendix P: Bulk Shipping Instructions

Appendix Q: UPS ShipExec™ Thin Client Instructions

# Appendix A – Whole Blood Collection for Isolation of RNA

**Whole Blood Collection for Isolation of RNA: 2.5 ml PAXgene® tubes are provided by BioSEND for the collection of blood for RNA isolation.**


See training video for blood collection for RNA: (http://www.preanalytix.com/videos/rna-tube-collection-video/)

1. **CRITICAL STEP: Store PAXgene® tube(s) at room temperature 64$^0$F - 77$^0$F (18°C to 25°C) before use.**

2. Place pre-printed Collection and Aliquot "**RNA**" label on the PAXgene® tube(s) prior to blood draw.


3. Using a blood collection set and a holder, collect blood into the PAXgene® tube(s) using your institution's recommended procedure for standard venipuncture technique.

**The following techniques shall be used to prevent possible backflow:**

a. Place donor's arm in a downward position.
b. Hold tube in a vertical position, below the donor's arm during blood collection.
c. Release tourniquet as soon as blood starts to flow into tube.
d. Make sure tube additives do not touch stopper or end of the needle during venipuncture.

4. Allow at least 10 seconds for a complete blood draw to take place in each tube. Ensure that the blood has stopped flowing into the tube before removing the tube from the holder. The PAXgene® tube with its vacuum is designed to draw 2.5 ml of blood into the tube.

5. Immediately after blood collection, gently invert/mix (180 degree turns) the PAXgene® tube(s) 8 – 10 times. Do not shake the tube!

6. Place the PAXgene® tube(s) upright in a wire or plastic rack. Do **NOT** use a Styrofoam rack. This will cause the PAXgene® tube(s) to crack when frozen. **Allow the filled PAXgene® tube(s) to incubate upright at room temperature for 2 hours.**

7. Complete the Sample Form for this collection.

8. After samples have incubated at room temperature for 2 hours, transfer the WIRE or PLASTIC rack with the PAXgene® tubes to **-80°C freezer**. Store all samples at -80°C until shipped to BioSEND on dry ice.

9. Ship the PAXgene® tubes to BioSEND according to **Appendix K - Frozen Shipping Instructions**.

# RNA Collection and Preparation – 2.5 ml PAXGene Tube

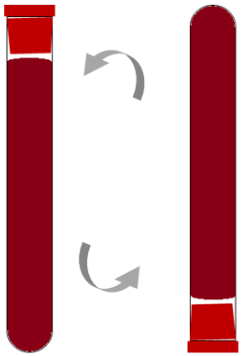
## Step One


- Store tubes at room temperature.
- Label tubes with preprinted RNA labels prior to draw.

## Step Two

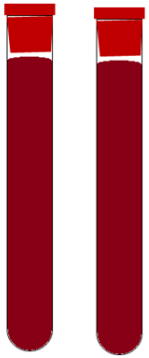
- Collect blood into PAXGene tubes, allowing blood to flow for 10 seconds and ensuring blood flow has stopped.

## Step Three



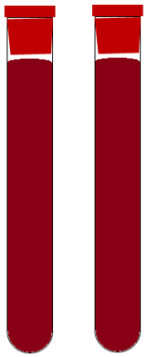
- Immediately after blood draw, invert tubes 8-10 times to mix samples.

## Step Four



- Incubate tubes upright at room temperature for 2 hours.

## Step Five



- After incubation period, freeze tubes upright in -80 in a **wire** rack. Keep frozen until shipment.

# Appendix B – Whole Blood Collection for Isolation of Plasma

**Whole Blood Collection for Isolation of Plasma: 10 ml Lavender-Top EDTA tube(s) and cryotubes are provided by BioSEND for the collection of plasma.**

1. **CRITICAL STEP: Store empty Lavender-Top EDTA tubes at room temperature 64°F – 77°F (18°C to 25°C) prior to use.**

2. Place pre-printed **PLASMA** label on 10 ml lavender-top EDTA tube and on six of the 0.5 ml cryotube tubes. Label one 2ml cryotube with a **BUFFY COAT** label. The seven labeled cryotubes will be shipped to BioSEND. The remaining plasma can be retained by the site and labeled per site standards. Labels for samples kept by the site are not provided by BioSEND.

3. Pre-chill the labeled cryotubes on wet ice for at least 5 minutes.

4. Set centrifuge to 4°C to pre-chill before use. Time needed to pre-chill the centrifuge to 4°C will depend on your centrifuge model.

5. Using a blood collection set and a holder, collect blood into the lavender top 10 ml EDTA tube(s) using your institution's recommended procedure for standard venipuncture technique.

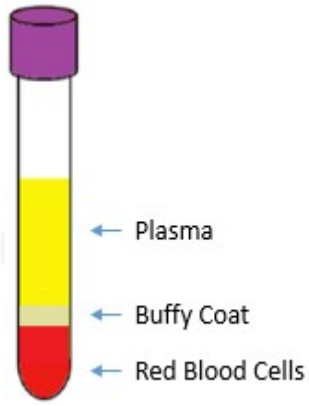
   The following techniques shall be used to prevent possible backflow:
   a. Place donor's arm in a downward position.
   b. Hold tube in a vertical position, below the donor's arm during blood collection.
   c. Release tourniquet as soon as blood starts to flow into the tube.
   d. Make sure tube additives do not touch stopper or end of the needle during venipuncture.

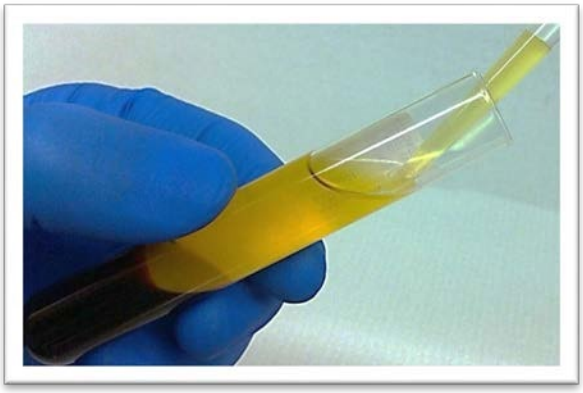
6. Allow at least 10 seconds for a complete blood draw to take place in each tube. Ensure that the blood has stopped flowing into the tube before removing the tube from the holder. The tube vacuum is designed to draw 10 ml of blood into the tube.

7. Immediately after blood collection, gently invert/mix (180 degree turns) the Lavender-Top EDTA tube(s) 8 – 10 times. Do not shake the tubes!

8. Within 30 minutes of blood collection, centrifuge balanced tubes for 15 minutes at 1500 RCF (x g) at 4°C. It is critical that the tubes be centrifuged at the appropriate speed and temperature to ensure proper plasma separation.

9. Remove the plasma by tilting the tube and placing the pipette tip along the lower side of the wall. **Use caution not to touch the buffy coat or packed red blood cells at the bottom of the tube so that the plasma is not contaminated** (see below). Using a disposable tipped micropipette, transfer plasma into the pre-labeled cryotubes. Aliquot 250 ul per cryotube. Send six 250ul aliquots to BioSEND. If you cannot obtain the requested number of aliquots, please note "low volume draw" on the Sample Form. Each 10 ml EDTA tube should yield, on average, 5 ml of plasma.



10. After plasma has been removed from the EDTA tube, aliquot buffy coat layer (see figure above) into labeled cryotube with clear cap using a disposable graduated micropipette. All of the buffy coat from a single 10 ml lavender-top EDTA tube will be placed into one cryotube. The buffy coat aliquot is expected to have a reddish color from the red blood cells.

11. Complete the Sample Form for this collection.

12. Place the labeled cryotubes in the 25 slot cryobox. Place the cryobox UPRIGHT on dry ice. Transfer to **-80°C freezer as soon as possible**. Store all samples at -80°C until shipped to BioSEND on dry ice.

13. Ship the frozen plasma and buffy coat aliquots to BioSEND according to **Appendix K – Frozen Shipping Instructions.**

# Plasma and Buffy Coat Preparation –10 ml EDTA (Purple Top) Tube

## Step One


- Store tubes at room temperature.
- Label tubes with preprinted plasma and buffy coat labels prior to blood draw.

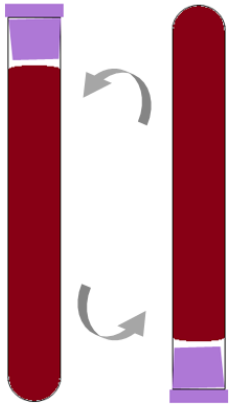
## Step Two

- Label six 0.5ml cryotubes with plasma labels and one 2ml cryotubes with buffy coat labels.
- Pre-chill cryotubes on wet ice for at least 5 minutes

## Step Three

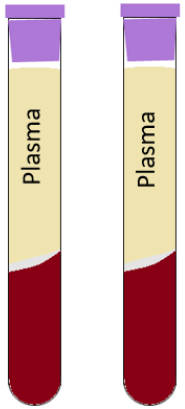
- Collect blood in EDTA tube, allowing blood to flow for 10 seconds and ensuring blood flow has stopped.

## Step Four



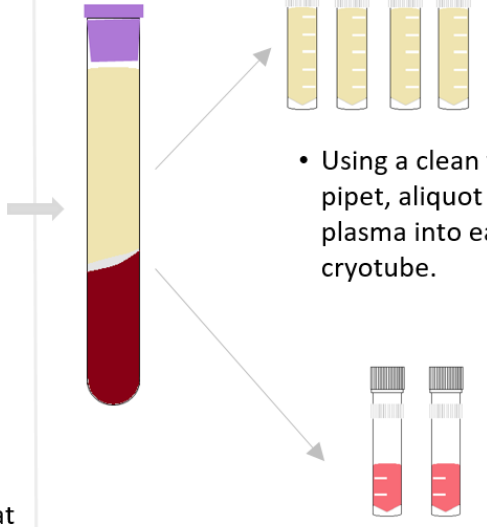
- Immediately after blood draw, invert tube 8-10 times to mix samples.

## Step Five




- Within 30 minutes of blood draw, centrifuge sample at <u>4°C</u> at <u>1500 x g</u> for <u>15 minutes</u>.

## Step Six



- Using a clean transfer pipet, aliquot 250ul plasma into each 0.5ml cryotube.
- After creating plasma aliquots, use a clean transfer pipet to collect the buffy coats (will include residual plasma and some red blood cells).
- Transfer each buffy coat to separate, 2ml cryotubes.
- Store plasma and buffy coat aliquots <u>upright</u> at -80°C until shipment.

# Appendix K – Frozen Shipping Instructions

**IMPORTANT!**

Frozen samples must be shipped Monday – Wednesday only, using Next Day Air delivery

Please be aware of holidays and inclement weather and plan your shipments accordingly. Reach out to biosend@iu.edu if you have any questions

Specimens being shipped to BioSEND are Category B UN3373 specimens and as such must be triple packaged and compliant with IATA Packing Instructions. *See the latest eEdition of the IATA regulations for complete documentation.*

Triple packaging consists of a primary receptacle(s), a secondary packaging, and a rigid outer packaging. The primary receptacles must be packed in secondary packaging in such a way that, under normal conditions of transport, they cannot break, be punctured, or leak their contents into the secondary packaging. Secondary packaging must be secured in outer packaging with suitable cushioning material. Any leakage of the contents must not compromise the integrity of the cushioning material or of the outer packaging.

## IATA Packing and Labeling Guidelines

- The primary receptacle (cryovials or blood collection tubes) must be leak proof and must not contain more than 1 L total.
- The secondary packaging (plastic canister or biohazard bag) must be leak proof and if multiple blood tubes are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent direct contact with adjacent blood tubes.
- Absorbent material must be placed between the primary receptacle (cryovials or blood collection tubes) and the secondary packaging. The absorbent material must be of sufficient quantity to absorb the entire contents of the specimens being shipped. Examples of absorbent material are paper towels, absorbent pads, cotton balls, or cellulose wadding.
- A shipping manifest listing the specimens being shipped must be included between the secondary and outer packaging.
- The outer shipping container must display the following labels:
  - ✓ Sender's name and address
  - ✓ Recipient's name and address
  - ✓ Responsible persons (shipper and recipient)
  - ✓ The words "Biological Substance, Category B"
  - ✓ UN3373
  - ✓ Class 9 label including UN 1845, and net weight of dry ice contained

## BioSEND Packaging and Shipment Instructions – Frozen Shipments

1. Generate airway bill and schedule courier pick-up, as needed.

    - For instructions on generating airway bills and scheduling using the UPS ShipExec™ Thin Client system, see Appendix Q.

2. Record the tracking number onto the Sample Record and Shipment Notification form (Appendix I).

3. Make a copy of the Sample Record and Shipment Notification form.

4. Place all frozen labeled cryotubes in the cryobox. Only include specimens from one subject in each cryobox.

5. Place the cryobox in a clear plastic biohazard bag (do NOT remove the absorbent material found in the bag), and seal the biohazard bag according to the instructions on the bag. Affix a Case Label to the outside of the biohazard bag.


6. Place approximately 2-3 inches of dry ice in the bottom of the Styrofoam® shipping container.

7. If your protocol is collecting frozen whole blood, DNA, or RNA, place labeled tubes in bubble sleeves and seal.

8. Place the tubes in a clear plastic biohazard bag (do NOT remove the absorbent material found in the bag), and seal the biohazard bag according to the instructions on the bag. Affix a Case Label to the outside of the biohazard bag.

9. Place the biohazard bag containing the cryobox into the provided Styrofoam® shipping container on top of the dry ice. Please ensure that the cryobox is placed so that the cryovials are upright in the shipping container (as pictured).

10. Fully cover the cryobox with approximately 2 inches of dry ice. Do not include more than 2 subjects' worth of samples in a single shipper.

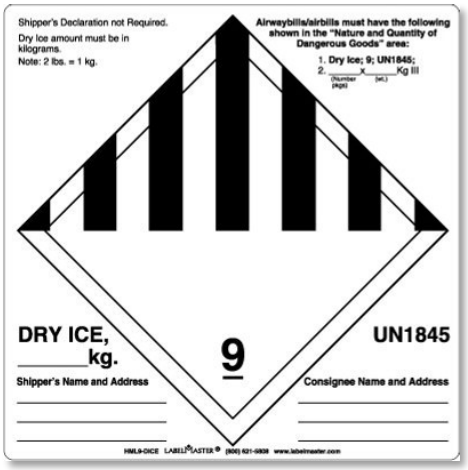
11. If including additional biohazard bags in package, include a layer of dry ice (approximately 2 inches) between each biohazard bag.

12. The inner Styrofoam® shipping container must contain approximately 10 lbs (or 4.5 kg) of dry ice. The dry ice should entirely fill the inner box to ensure the frozen state of the specimens.

13. Replace the lid on the Styrofoam® container. Place the completed Sample Record and Shipment Notification form in the package on top of the Styrofoam® lid for each patient specimen, and close and seal the outer cardboard shipping carton with packing tape.

14. Print a copy of your UPS® airway bill generated through the UPS ShipExec™ Thin Client system (see Appendix Q). Place airway bill into the provided airway bill envelope and affix envelope to package.

15. Complete the Class 9 UN 1845 Dry Ice Label (black and white diamond) with the following information:
    - Your name and return address
    - Net weight of dry ice in kg (this amount must match the amount recorded on the airway bill)
    - Consignee name and address:

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Indianapolis, IN 46202

- Do not cover any part of this label with other stickers, including pre-printed address labels.

| **IMPORTANT!** |
| --- |
| Complete the required fields on your airway bill and Class 9 Dry Ice labels, or courier may reject or return your package. |

16. Apply all provided warning labels (UN3373, Dry Ice Label and Fragile Label), taking care not to overlap labels with each other or with airway bill.

17. Hold packaged samples in -80°C freezer until time of courier pick-up/drop-off.

18. Specimens should be sent to the address below. Frozen shipments should be sent Monday through Wednesday only to avoid shipping delays on Thursday or Friday.

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19. **Notify BioSEND by email (biosend@iu.edu) that a shipment has been sent and attach the Sample Record and Shipment Notification form to your email. Do not ship until you've contacted and notified BioSEND staff about the shipment in advance.**

20. Use courier tracking system to ensure the delivery occurs as scheduled and is received by BioSEND.

In addition to tracking and reconciliation of samples, the condition and amount of samples received are tracked by BioSEND for each sample type. Investigators and clinical coordinators for each project are responsible for ensuring that the requested amounts of each fluid are collected to the best of their ability and that samples are packed with sufficient amounts of dry ice to avoid thawing in the shipment process.

# Appendix P– Bulk Frozen Shipping Instructions

Use these instructions when shipping samples from multiple subjects and potentially multiple draw dates, together in one shipment container. Please discuss the option of bulk shipping with BioSEND before using this method.

| IMPORTANT! |
| --- |
| Frozen must be shipped **Monday through Wednesday only**, using overnight delivery service.<br><br>Please be aware of holidays and inclement weather, and plan your shipments accordingly. Contact biosend@iu.edu if you have any questions. |

Specimens being shipped to BioSEND are Category B UN3373 specimens and as such must be triple packaged and compliant with IATA Packing Instructions. *See the latest eEdition of the IATA regulations for complete documentation.*

Triple packaging consists of a primary receptacle(s), a secondary packaging, and a rigid outer packaging. The primary receptacles must be packed in secondary packaging in such a way that, under normal conditions of transport, they cannot break, be punctured, or leak their contents into the secondary packaging. Secondary packaging must be secured in outer packaging with suitable cushioning material. Any leakage of the contents must not compromise the integrity of the cushioning material or of the outer packaging.

## IATA Packing and Labeling Guidelines

- The primary receptacle (cryovials or blood collection tubes) must be leak proof and must not contain more than 1 mL total.
- The secondary packaging (plastic canister or biohazard bag) must be leak proof and if multiple blood tubes are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent direct contact with adjacent blood tubes.
- Absorbent material must be placed between the primary receptacle (cryovials or blood collection tubes) and the secondary packaging. The absorbent material must be of sufficient quantity to absorb the entire contents of the specimens being shipped. Examples of absorbent material are paper towels, absorbent pads, cotton balls, or cellulose wadding.
- A shipping manifest listing the specimens being shipped must be included between the secondary and outer packaging.
- The outer shipping container must display the following labels:
  - ✓ Sender's name and address
  - ✓ Recipient's name and address
  - ✓ Responsible persons (shipper and recipient)
  - ✓ The words "Biological Substance, Category B"
  - ✓ UN3373
  - ✓ Class 9 label including UN 1845, and net weight of dry ice contained

## BioSEND Packaging and Shipment Instructions – Bulk Frozen Shipments

1. Generate airway bill and schedule courier pick-up, as needed.
   - ➢ For instructions on generating airway bills and scheduling using the UPS ShipExec™ Thin Client system, see Appendix Q.

2. Record the tracking number onto the sample form. The tracking number must be included with your shipping notification to BioSEND.

3. Make a copy of the Sample Record and Shipment Notification form.

4. Place all frozen, labeled aliqouts in the cryobox.
   - ➢ Each cryobox holds 25 aliquots. Only include specimens from one subject in each cryobox.

5. Place the cryobox in the clear plastic biohazard bag (do NOT remove the absorbent material found in the bag), and seal the biohazard bag according to the instructions on the bag. Affix a Case Label to the outside of the biohazard bag.

6. Insert PAXgene™ tube(s) into the bubble wrap tube shuttle, and place the tube shuttle(s) in the 2nd plastic biohazard bag. Seal the biohazard bag according to the instructions on the bag. Affix a Case Label to the outside of the biohazard bag.

7. Place approximately 2-3 inches of dry ice in the bottom of the large Styrofoam shipping container.

8. Place the biohazard bag containing the cryobox into the provided Styrofoam® shipping container (large) on top of the dry ice. Please ensure that the cryobox is placed so that the cryovials are upright in the shipping container. **Please include only 5-10 cryoboxes.**

9. Fully cover the cryobox with approximately 2 inches of dry ice.

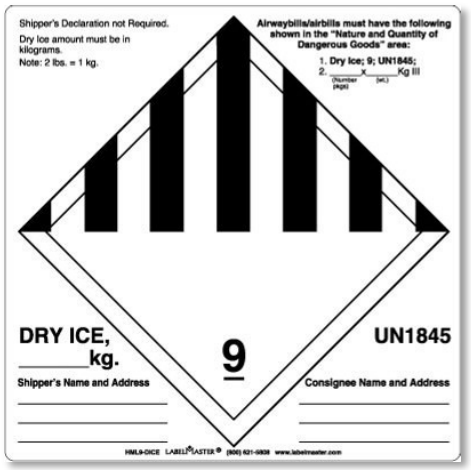
10. Place the biohazard bag containing the PAXgene™ tubes on top of the 2nd layer of dry ice and cover with another 2-3 inches of dry ice. **Please include only 5-10 biohazard tube bags.**

11. The inner Styrofoam® shipping container must contain approximately 30-40 lbs (or 20 kg) of dry ice. The dry ice should entirely fill the inner box and be placed on top of the bags to ensure the frozen state of the specimens.

12. Replace the lid on the Styrofoam® container. Place the completed Sample Record and Shipment Notification form in the package on top of the Styrofoam® lid for each patient specimen, and close and seal the outer cardboard shipping carton with packing tape.

13. Print a copy of your UPS® airway bill generated through the UPS ShipExec™ Thin Client system (see Appendix Q). Place airway bill into the provided airway bill envelope and affix envelope to package.

14. Complete the Class 9 UN 1845 Dry Ice Label (black and white diamond) with the following information:
    a. Your name and return address
    b. Net weight of dry ice in kg (this amount must match the amount recorded on the airbill)
    c. Consignee name and address:

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    d. Do not cover any part of this label with other stickers, including pre-printed address labels.

| **IMPORTANT!** |
| --- |
| Complete the required fields on your airway bill and Class 9 Dry Ice labels, or courier may reject or return your package. |

15. Apply all provided warning labels (UN3373, Dry Ice Label and Fragile Label), taking care not to overlap labels with each other or with airway bill.

16. Hold packaged samples in -80°C freezer until time of courier pick-up/drop-off.

17. Specimens should be sent to the address below. Frozen shipments should be sent Monday through Wednesday only to avoid shipping delays on Thursday or Friday.

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18. **Notify BioSEND by email (biosend@iu.edu) that a shipment has been sent and attach the Sample Record and Shipment Notification form to your email. If email is unavailable please call BioSEND. Do not ship until you've contacted and notified BioSEND staff about the shipment in advance.**

19. Use courier tracking to ensure the delivery occurs as scheduled and is received by BioSEND.

In addition to tracking and reconciliation of samples, the condition and amount of samples received are tracked by BioSEND for each sample type. Investigators and clinical coordinators for each project are responsible for ensuring that the requested amounts of each fluid are collected to the best of their ability and that samples are packed with sufficient amounts of dry ice to avoid thawing in the shipment process.

| **IMPORTANT!** |
| --- |
| **Bulk frozen shipments, should include no more than ten cryovial boxes (separated by patient within biohazard bags) and ten biohazard tube bags per shipping container in order to have room for a sufficient amount of dry ice to keep samples frozen up to 24 hours.** |

# Appendix Q - UPS ShipExec™ Thin Client Instructions

1) Log in to the UPS ShipExec™ Thin Client website: https://kits.iu.edu/UPS or https://kits.iu.edu/ups.
    a. To request an account, complete the following survey: https://redcap.uits.iu.edu/surveys/?s=88TTWY3KAF
2) Find the "Shipping" dropdown menu in the top left corner of the screen and click on "Shipping and Rating".
3) Once the Indiana University page loads, look for the "Study Group" dropdown menu under "Shipment Information" on the right side of the screen. Choose your study from the dropdown menu.
4) After selecting your study, click on the magnifying glass icon on the left side of the screen under "Ship From".
5) An address book and filters will populate the screen. On the right side of the screen, a list of all the site addresses within the study you selected should populate.
    a. Filter the list down more by looking to the left side of the screen and searching for their address by filling in the "Company", "Contact", or "Address 1" fields. Click on the Search button when ready.
    b. Once you have found your site address, click on the "Select" button to the left of the address.
6) Make sure your address populated in the fields under "Ship From" on the main page.
    a. If you accidentally selected the wrong address, click on the "Reset" button on the bottom right of the screen. After the page reloads and clears the information, select your study again from the "Study Group" menu and click on the magnifying glass icon again to search for your correct address.
    b. To change the address for your site and study group, please complete the following survey: https://redcap.uits.iu.edu/surveys/?s=88TTWY3KAF
7) Enter the total weight of your package in the "Weight" field on the right side of screen under the name of your study.
    a. Leave the "Dry Ice Weight" field empty or enter "0" if shipping an ambient sample.
8) Enter the weight of the dry ice for frozen shipments in the "Dry Ice Weight" field.
    a. The "Dry Ice Weight" field can *never* be higher than the "Weight" field.
    b. **(Steps 9-10 can be skipped if you do not need to schedule a pickup)**
9) After entering the weights, click on the blue "Pickup Request" button.
10) When the Create Pickup Request box pops up, enter information into all the fields provided.
    a. Enter the "Earliest Time Ready" and "Latest Time Ready" in 24-hour format.
        i. Scheulde pickup at a minimum 1 hour *before* the "Earliest Time Ready"
    b. Choose a name and phone number that is the best contact if the UPS driver has question related to picking up your package
    c. Entering the "Room Number" and "Floor" will help the UPS driver locate your package
        i. The "Floor" field only allows numerical characters while the "Room Number" field is free text.
    d. Click "Save" when done.
11) Once you are certain that all the correct information has been entered, click the "Ship" button in the bottom right corner of the screen.
12) If no red error messages pop up at the top of your screen after clicking on "Ship", then you should have 2 downloaded PDF files: Shipment Receipt & UPS Package Label

   a. Shipment Receipt will list a “Pickup No.” that references your specific package if there is ever an issue with UPS picking up your package

13) Print out the UPS airway bill to any printer at your location.
   a. Fold the UPS airway bill and slide it inside the plastic UPS sleeve.
   b. Peel the back off the plastic UPS sleeve and stick the sleeve to your package, making sure it is laying as flat as possible along the surface of the package.
14) Place your package in the spot designated in your pickup request, or wherever your daily UPS pickups occur.
15) If you need to reprint your airway bill or void your shipment, click on “History” at the top of the main screen.
   a. If your shipment does not automatically pop up, enter the date of shipment and then click “Search”.
   b. To reprint your airway bill, click on the printer icon to the far left under “Action”
   c. To void your shipment, click on the “X” icon to the far left under “Action”
      i. If you created an airway bill that you no longer need, you must void the shipment to ensure your study will not be charged for the shipment.