

National Institute of Neurological Disorders and Stroke
Biorepository:

BioSpecimen Exchange for Neurological Disorders, BioSEND

Biospecimen Collection, Processing, and Shipment Manual for

NINDS Udall Centers of Excellence for

Parkinson's Disease Research:

University of Michigan

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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 and shipping of the following samples:

- DNA (from whole blood)

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
RBC	Red Blood Cells
RCF	Relative Centrifugal Force
RPM	Revolutions Per Minute

3.0 BioSEND INFORMATION

3.1 BioSEND Contacts

Tatiana Foroud, PhD, Principal Investigator

Phone: 317-274-2218

Email: tforoud@iu.edu

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.

Ambient samples must be shipped Monday- Thursday only.

For packaging and shipment details, please refer to Appendix L (Ambient 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 website.

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
3 rd Monday in January	Martin Luther King, Jr Day
4 th Monday in May	Memorial Day
June 19 th	Juneteenth (observed)
July 4 th	Independence Day (observed)
1 st Monday in September	Labor Day
4 th Thursday in November	Thanksgiving
4 th 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.

Please see https://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 4.1-4.2](#).

If a sample is not obtained at a particular visit, this should be recorded in the notes section of the **Sample Record and Shipment Notification Form (see Appendix I)**. These forms are submitted with your sample shipment to BioSEND.

4.1 Protocol Schedule for Biospecimen Submission to BioSEND-Udall Michigan

Sample Type	BL
DNA, 6ml	2

5.0 SPECIMEN COLLECTION KITS, SHIPPING KITS AND SUPPLIES

Research specimen collection kits as well as clinical lab supplies (except equipment listed in Section 5.7) will be provided by BioSEND. These materials include blood tubes, specimen labels, and shipping supplies needed to send materials to BioSEND. 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 4.1-4.2](#)); 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

Each individual site will be responsible for ordering kits 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 site institution. Kits and individual items can be ordered as required through the kit request module.

The link to the kit request module is shown below:

- Udall: <http://kits.iu.edu/biosend/udall>

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 can be provided should you require additional supplies from those contained in the visit specific kits. Replacement supplemental kits can be requested on the kit request website. In addition, individual supplies can be requested as well.

BioSEND Supplies

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

General Items
Airway bill envelope
Shipping container for ambient shipments (outer cardboard and inner Styrofoam® box)
UPS Overpak
Plastic biohazard bag with absorbent sheet
Blood Collection Items
EDTA blood collection tubes (plastic, 6ml)

5.3 Specimen Collection Kit Contents – Udall Minnesota

Udall Minnesota Baseline Collection Kit	
Supply	Amount
EDTA (palstic) tube, 6ml	2
Biohazard bag w/ absorbent sheet	1
UN3373 label	1
Refrigerant Pack	1
Airway bill envelope	1
Ambient shipper	1
Label set (case & specimen labels)	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**:

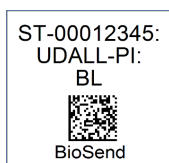
- Personal Protective Equipment: lab coat, nitrile/latex gloves, safety glasses
- Tourniquets
- Alcohol Prep Pads
- Gauze Pads
- Bandages
- Butterfly needles and hubs

6.0 SPECIMEN LABELS

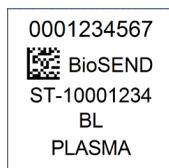
Labels must be affixed on all collection tubes to ensure unique specimen identity. BioSEND provides labels for all samples being collected and returned to BioSEND. The site is responsible for providing labels for biospecimens that will be retained at the site.

6.1 Types of Labels

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. See Appendix L for further instructions.

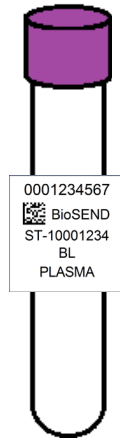


The **Specimen Labels** are placed on all blood collection tubes. See Appendix E for further instructions.

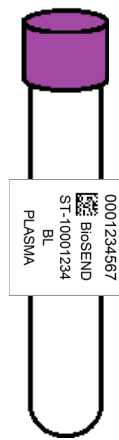
6.2 Affixing Labels

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

- Place specimen labels on **ALL** collection tubes and **BEFORE** sample collection. This will help to ensure the label properly adheres to the tube before exposure to moisture or different temperatures.
- The specimen 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); see below.



Incorrect



Correct

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 Draw for BioSEND Collection Tubes

1. EDTA (purple top, 6ml) x 2 for DNA

7.2 Blood Collection Protocols

1. Whole Blood Collection for Isolation of DNA (Appendix E)

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 Sample Record and Shipment Notification Form

All sample shipments to BioSEND must include the BioSEND Sample Record and Shipment Notification Form. The completed forms should be:

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

8.2 Shipping Instructions

Reference Appendix L for ambient shipping instructions.

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 Data Queries and Reconciliation

Appendix I must be completed the day that samples are collected to capture information related to sample collection and processing. This form includes information that will be used to reconcile sample collection and receipt, as well as information essential to future analyses.

The NINDS DMR data collection team will be collaborating with BioSEND to reconcile information captured in the database compared to samples received and logged at BioSEND. Information that appears incorrect in the clinical database will be queried through the standard system. Additional discrepancies that may be unrelated to data entry will be resolved with the Principal Investigator in a separate follow up communication. If applicable, a non-conformance report will be provided to sites.

Data discrepancies with samples shipped and received at BioSEND may result from:

- Missing samples
- Incorrect samples collected and shipped
- Damaged or incorrectly prepared samples
- Unlabeled or mislabeled samples
- Discrepant information reported in the clinical database compared to information on Appendix I
- Samples frozen and stored longer than three months at the site

10.0 APPENDICES

Appendix E: Whole Blood Collection for Isolation of DNA

Appendix I: Sample Record and Shipment Notification Form

Appendix L: Ambient Shipping Instructions

Appendix Q: UPS ShipExec™ Thin Client Instructions

Appendix E – Whole Blood Collection for Isolation of DNA (No Processing)

Two 6 ml Purple-Top EDTA Tubes are provided by BioSEND for the collection of Whole Blood from which DNA will be extracted. This tube should be shipped to BioSEND at AMBIENT temperature on the day it is drawn (no processing required).



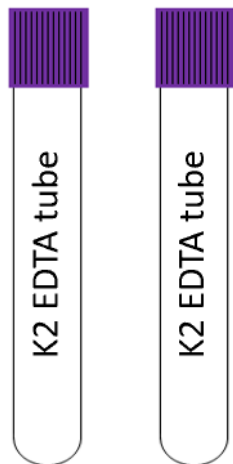
1. Store empty Whole Blood EDTA tubes at room temperature, 64°F - 77°F (18°C to 25°C) before use.
2. Place pre-printed Collection and Aliquot “DNA” label on the **6 ml EDTA tubes** prior to blood draw.
3. Using a blood collection set and a holder, collect whole blood into the 6 ml EDTA tubes using your 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. Immediately after blood collection, gently invert/mix (180 degree turns) the EDTA tube 3 times.
 5. Complete the **Sample Record and Shipment Notification form Appendix I).**
 6. Ship the whole blood tube for DNA extraction to BioSEND according to **Appendix L – Ambient Shipping Instructions.**

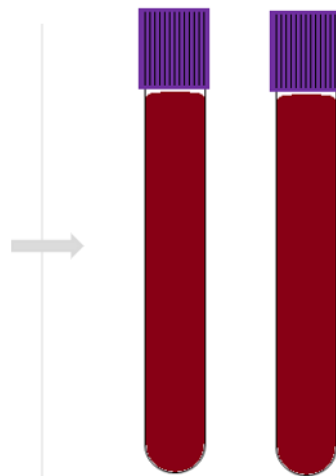
DNA Preparation – 6 ml K2 EDTA (Purple Top) Tube

Step One



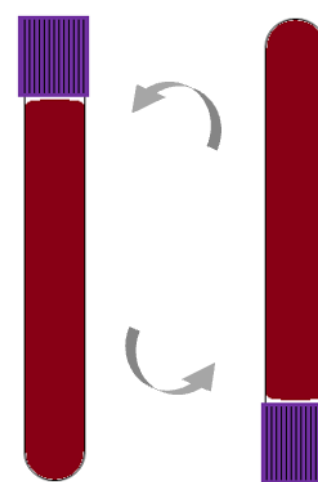
- Store tubes at room temperature.
- Label tubes with DNA specimen labels prior to blood draw.

Step Two



- Collect blood in K2 EDTA tubes, allowing blood to flow for 10 seconds and ensuring blood flow has stopped.

Step Three



- Immediately after blood draw, invert tubes 3 times to mix samples.

Step Four



- Keep samples at ambient temperature until ready to ship. Sample must be received at BioSEND within 5 days of collection.

Sample Record and Shipment Notification

Study:	<input type="text"/>		
Site Name:	<input type="text"/>	Principal Investigator:	<input type="text"/>
Coordinator:	<input type="text"/>	Telephone:	<input type="text"/>
		Email:	<input type="text"/>

Please list only ONE subject per Sample Record Summary and Shipment Notification Form

GUID:	<input type="text"/>	Subject ID (ST# from pre-printed labels):	<input type="text"/>
Sex:	<input type="text"/>	Visit Type:	<input type="text"/>

Instructions: Ship Frozen Shipments Monday- Wednesday. Ambient Shipments may be shipped Monday- Thursday provided they are received at Indiana University within five days of collection. This form must be completed for shipment of all research samples. Notify Indiana University at biosend@iu.edu and the DMR in advance of shipment. Place a copy in the shipment box. Ensure all frozen shipments are completely filled with dry ice.

Date Sample(s) Shipped:	<input type="text"/>	Tracking Number:	<input type="text"/>
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Completed by Submitter/Site			
Dates of Draw	Specimen Type	Number of Tubes/ Aliquots sent to BioSEND	Notation of Problems
	DNA		
	RNA		
	Buffy Coat		
	Plasma		
	Serum		
	CSF		
	Whole Blood		

**Contact Information: Indiana University; Email: biosend@iu.edu Ph: 317-278-0594
Data Management Resource (DMR); Email: PDBP-OPS@mail.nih.gov**

Appendix L – Ambient Shipping Instructions

IMPORTANT!

Ambient samples must be shipped Monday – Thursday 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

Ambient whole blood tube shipments are Category B UN3373 and as such must be triple packaged and compliant with IATA Packing Instructions. *See the latest edition 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 should 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

BioSEND Packaging and Shipment Instructions – Ambient Shipments

1. Place refrigerant pack in the freezer 24 hours before shipment.
2. 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.
3. Record the tracking number onto the Sample Record and Shipment Notification form (Appendix I).
4. Make a copy of the Sample Record and Shipment Notification form.
5. Place filled and labeled EDTA tube(s) in the biohazard bag with the absorbent material.
6. Remove as much air as possible from the biohazard bag, and seal the bag according to the directions on the bag. Place Case Label on outside of biohazard bag.



7. Place the specimen into the Styrofoam cooler, and then place the refrigerant pack on top of the specimen.
8. Place a copy of the Sample Record and Shipment Notification form and a completed IATA List of Contents sheet (provided in kit) on top of the cooler and close the cardboard box. Please do NOT tape the cardboard box closed.
9. Close shipping box and place within the provided overpack and seal.
10. Affix airway bill to the sealed overpack.
11. Specimens should be sent to the address below. Shipments should be sent Monday through Thursday.

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

12. **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.**

13. Use courier tracking number 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.

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. Schedule 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.