

National Institute of Neurological Disorders and Stroke
Biorepository:

BioSpecimen Exchange for Neurological Disorders, BioSEND

Biospecimen Collection, Processing, and Shipment Manual

**Morris K. Udall Centers of Excellence for Parkinson's Disease
Research**

Baseline Visit Only

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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:

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

3.0 BioSEND INFORMATION

3.1 BioSEND Contacts

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Email: tforoud@iu.edu

Scott Kaiser, Project Manager

Phone: 317-278-0594

Email: sckaiser@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

980 W. Walnut Street , R3 C158

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 packing and shipment details, please refer to Appendix L (Ambient Shipping Instructions).

Check the weather reports and the FedEx.com website to make sure impending weather events (blizzards, hurricanes, etc.) will not impact the shipping or delivery of the samples. FedEx often reports 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
July 4	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. 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 January 2nd.

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 [section 4.1](#).

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)**. This form is submitted with your sample shipment to BioSEND.

4.1 Protocol Schedule for Biospecimen Submission to BioSEND - Udall Centers, Baseline only

Visit (month)	BL	6	12	18	24	30	36	42	48	54	60
Blood sample for DNA (EDTA tube, 6ml)	1										

5.0 SPECIMEN COLLECTION KITS, SHIPPING KITS AND SUPPLIES

Research specimen collection kits as well as clinical lab supplies will be provided by BioSEND. These materials include blood tubes and partially completed shipping labels to send materials to BioSEND. Barcoded kit labels and collection tube labels will be provided by BioSEND. Collection 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

Each individual site will be responsible for ordering and maintaining a steady supply of kits from BioSEND. We advise sites to keep a supply of each kit type available. Be sure to check your supplies and order additional materials before you run out so that you are prepared for study visits.

There are unique kit request modules for each study site. Within each kit request module, there is a drop down to request kits for a particular study site based upon the name of the Principal Investigator at that site. Kit options include ordering a specific number of kits (baseline visit or supplemental kit); we are also including the option of simply ordering the desired amount of extra supplies.

The link to each kit request module is shown below:

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

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. See the next page for LP Kit contents.

BioSEND Supplies

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

General Items
Ambient shipping kits
FedEx return airbill
Plastic biohazard bag
Warning label packet
Blood Collection Items
Purple-top EDTA blood collection tube (6 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 – Udall Centers

Specimen Collection Supplies	PAXgene (2.5ml)	EDTA (10ml)	Serum (10ml)	EDTA (6ml)	Cryovial (2ml)	LP Tray (24 or 22 gauge)	Conical Tube (15ml)	Conical Tube (50ml)	Ambient Shipping Kit	Frozen Shipping Kit	Site specific supplies
Initial Visit				1					1		

5.4 Site Required Equipment

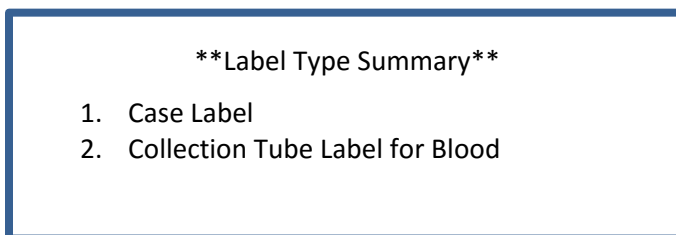
The following materials and equipment are necessary for the processing of specimens at the collection site and are to be **supplied by the local site**:

- 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

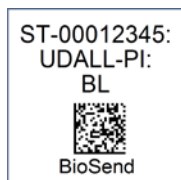
6.0 SPECIMEN LABELS

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. **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.**

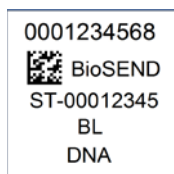
6.1 Types of Labels



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 Appendices I-L for further instructions.



The **Collection Tube Labels for Blood** are placed on all blood collection tubes. See [Appendix E](#) for further instructions.

6.2 Affixing Label

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

- Place blood collection label on collection tube **BEFORE** sample collection. This will help to ensure the label properly adheres to the tube before exposure to moisture or different temperatures.
- The blood collection tube label 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 labeling diagram).



- Take a moment to ensure the label is **completely affixed** to 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. **Please read the instructions before collecting any specimens. Have all your supplies and equipment out and prepared prior to drawing blood.**

7.1 Blood Collection Protocols

1. EDTA (purple top) blood collection for 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 Blood Processing Form(s). The completed form is:

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

8.2 Shipping Instructions

All samples will be returned to BioSEND in an ambient shipper. Reference Appendix L for ambient shipping instructions.

Ambient (room temperature) Shipment

- Blood sample for DNA (EDTA tube, 6 ml)

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

Include samples for only one subject per shipping container.

Ambient shipments (purple top EDTA tube) must be received at BioSEND within five days of collection. Up to three purple top EDTA tubes can be shipped in one ambient shipping container.

8.3 Shipping Address

All samples are shipped to the BioSEND laboratory:

BioSEND
Indiana University School of Medicine
980 W. Walnut Street, R3 C102
Indianapolis, IN 46202-5188

9.0 Data Queries and Reconciliation

The Sample Record and Shipment Notification Form (Appendix I) must be completed the day that samples are collected to capture information related to sample collection. This form includes information that will be used to reconcile sample collection and receipt.

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 NINDS DMR 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 documented on the BioSEND Blood Processing Forms compared to information entered into the NINDS DMR database.

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 O: Low Fat Diet Menu Suggestions

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

One 6 ml Purple-Top EDTA Tube is 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. **CRITICAL STEP:** 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 tube prior to blood draw.
3. Using a blood collection set and a holder, collect whole blood into the 6 ml purple top whole blood tube 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. **CRITICAL STEP:** Immediately after blood collection, gently invert/mix (180 degree turns) the EDTA tube 8-10 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 Lavender Top Tube)



Step One



- Store tube at room temperature.
- Label tube with pre-printed labels prior to blood draw.

Step Two



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

Step Three



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

Step Four



- Hold the specimen at room temperature until shipment BioSend.

Sample Record and Shipment Notification

Study:

Site Name: Principal Investigator:

Coordinator: Telephone: Email:

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

GUID: Subject ID (ST# from pre-printed labels):

Gender: Visit Type:

Age in Years: Plus Months:

Instructions: Ship Frozen Shipments Monday- Wednesday ONLY! Ambient Shipments (purple-top EDTA tube) may be shipped Monday- Thursday (preferably Monday- Wednesday) 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 (email preferred) and the DMR in advance of shipment using contact information below. Place a copy in the shipment box and file a copy of the completed form in the study binder. **Ensure all frozen shipments are completely filled with dry ice.**

Date Sample(s) Shipped: FedEx Tracking Number:

In the table below, please indicate the date of specimen collection and number of tubes/aliquots submitted.

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 THROUGH THURSDAY ONLY!

Please do NOT draw blood for ambient shipments on Fridays.

Please be aware of holidays and inclement weather, and plan your shipments accordingly.

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. Contact FedEx to confirm service is available and schedule package to be picked up.
2. **Record the FedEx tracking number (found at the top of the FedEx airbill) onto the Sample Record and Shipment Notification form (Appendix I).**
3. Make a copy of the Sample Record and Shipment Notification form.
4. Place filled and labeled EDTA tube within a slot in the absorbent tube shuttle provided. This tube and absorbent material is then placed within an IATA compliant plastic shipping canister. Replace canister lid and tighten.
5. Place Case Label on top of the tightened canister lid.



6. Wrap plastic canister in the provided bubble wrap.
7. Place the bubble wrapped canister in the provided small Shipping Box.
8. Place a copy of the Sample Record and Shipment Notification form within the shipping box.



9. Close shipping box and place within a Fed-Ex Clinical Pak. **Seal the Fed-Ex Clinical Pak.**
10. Affix prefilled FedEx return airbill to the sealed Fed-Ex Clinical Pak. Be sure to complete the FedEx return airbill with the following information: Section 1, "From": fill in the date, shipper's name, and phone number.
11. Specimens should be sent to the address below via **FedEx Priority Overnight**. Ambient FedEx shipments should be sent Monday through Thursday.



BioSEND
IU School of Medicine
980 W. Walnut Street, R3-C158
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. If email is unavailable please call BioSEND. Do not ship until you've contacted and notified BioSEND staff about the shipment in advance.**
13. Use FedEx 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.

Appendix O – Low Fat Diet Menu Suggestions

Foods to avoid prior to blood collection:

Avoid: *All fats and nuts such as:*

- Butter
- Cream
- Bacon fat
- Lard
- All oils
- All margarine
- All nuts
- Peanut butter
- Coconut
- Whole seeds such as pumpkin and sunflower

Avoid: *All milk and dairy products such as:*

- All whole milk products
- All cheese
- All products containing cheese
- Sour cream
- All ice cream
- Milk chocolate

Avoid: *High fat prepared foods and foods naturally high in fat:*

All red meats or meats containing fat
such as pork and:

- Fatty meats such as:
 - Luncheon meats
 - Organ meats
 - Bacon
- Fatty fish such as:
 - Salmon
 - Mackerel

-
- Salad dressing and mayonnaise
 - Fried foods
 - Fried snacks such as:
 - Chips
 - Crackers
 - French Fries
 - Buttered, au gratin, creamed, or fried vegetables
 - Gravies and sauces
 - Baked goods and frosting