



Biospecimen Exchange for Neurological Disorders

Emory LBD Study
PDBP Study ID 283

BIOSPECIMEN COLLECTION & PROCESSING

Overview

1. Specimen uniformity and quality
2. Site Equipment
3. Procedures
 - Kit Contents and Ordering
 - Sample Labelling
 - Sample Collection and Processing
 - Shipping Samples
 - Non-Conformance
4. Contact Information

Specimen Uniformity and Quality

GENERAL REMINDERS

Specimen Standardization and Quality

Most biomarkers are sensitive to *time* and *temperature*

- Standardization of processing across sites is key
- Specimens must be processed within 2 hours of collection
- Reference the *BioSEND Biomarker Specimen Collection, Processing, and Shipment Manual* as needed
- Do not replace or supplement any kit components without first receiving approval from BioSEND/NINDS

Questions? Email biosend@iu.edu

Site Consumables and Equipment

Sites will need to supply the following items:

- Gloves
- Alcohol wipes
- Butterfly needles
- Tourniquet
- Gauze pads
- Bandages
- Microcentrifuge tube rack
- Sharps bin and lid
- Crushed ice
- Pipettes and pipette tips
- Centrifuge capable of maintaining 4°C
- -80°C Freezer
- Dry ice

Procedures

MAINTAINING SPECIMEN UNIFORMITY AND QUALITY

Biospecimen Collection Protocol

	BL	12M	24M	36M	48M
Buffy coat (2 aliquots)	X	X	X	X	X
Plasma (6 x 1ml)	X	X	X	X	X
Serum (6 x 1ml)	X	X	X	X	X
RNA (2 x 2.5ml)	X	X	X	X	X
Whole Blood (1 x 3ml)	X	X	X	X	X
CSF (10 x 1ml)	X		X		X

Kit Contents and Ordering

- All sites will be sent a Supplemental Kit with their first kit shipment
 - Contains extra blood collection tubes, processing supplies, and LP needles
 - May be used to replace items in study visit kits
- Study Visit Kits should be ordered as soon as visits are planned
 - Contains collection, processing, and shipping supplies specific to each visit
 - Includes barcoded labels
 - The supplies/labels in each study visit kit are intended for that visit only

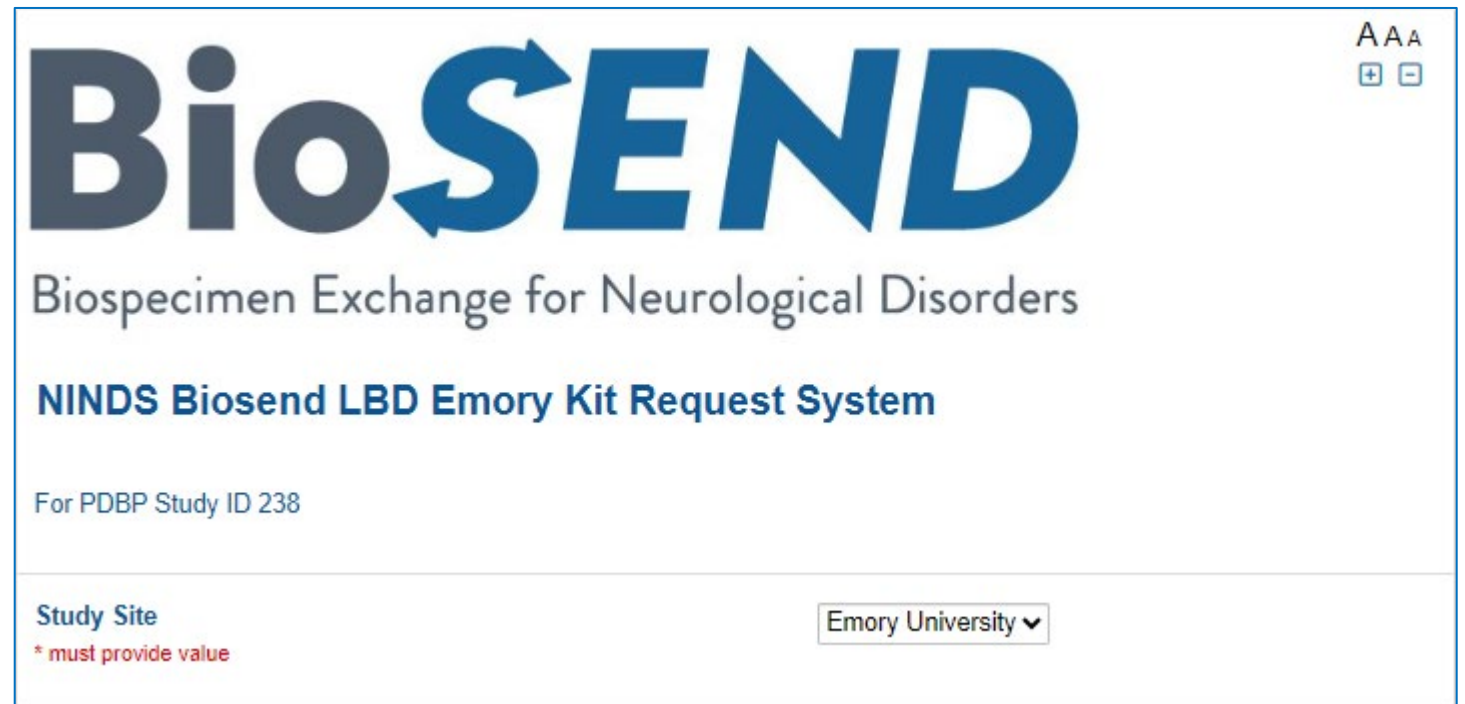
Kit Contents and Ordering – REDCap Survey

- <http://kits.iu.edu/biosend/EmoryLBD>

Order kits online through the Kit Request Module for:

- Blood & CSF kits
- Extra Supplies

Please provide as much notice as possible when ordering kits and/or supplies.

The image is a screenshot of a web application titled "BioSEND". The logo "BioSEND" is in large blue letters, with the "S" stylized as a circular arrow. Below the logo, it says "Biospecimen Exchange for Neurological Disorders". Underneath that is the title "NINDS Biosend LBD Emory Kit Request System". Further down, it specifies "For PDBP Study ID 238". At the bottom, there is a section labeled "Study Site" with a red asterisk and the text "* must provide value". To the right of this label is a dropdown menu currently showing "Emory University". In the top right corner of the interface, there are three small icons: "A A A" and two square buttons with "+" and "-" signs respectively.

BioSEND
Biospecimen Exchange for Neurological Disorders
NINDS Biosend LBD Emory Kit Request System
For PDBP Study ID 238
Study Site
* must provide value
Emory University ▼

Kit Contents and Ordering: Confirm Site Info

LBD Kit Request Module

Study Site <small>* must provide value</small>	Indiana University	Select your site from the drop-down list
Indiana University School of Medicine Carolyn Dunifon Dept. of Medical & Molecular Genetics 351 West 10th Street, TK-318 Indianapolis, IN 46202-3002 (317) 274-5751 cdunifon@iu.edu		
Verify contact information and update if needed		
Is the contact name above correct? <small>* must provide value</small>	<input type="radio"/> Yes <input checked="" type="radio"/> No	reset
New Contact Name <small>* must provide value</small>		
Claire Wegel		
Is the shipping address above correct? <small>* must provide value</small>	<input type="radio"/> Yes <input type="radio"/> No	reset
Is the e-mail address above correct? <small>* must provide value</small>	<input type="radio"/> Yes <input type="radio"/> No	reset
Is the phone number above correct? <small>* must provide value</small>	<input type="radio"/> Yes <input type="radio"/> No	reset

Kit Contents and Ordering: Kit Types

LBD Kit Request Module

- Kits are not specific to a subject or time point. After collection, sites will indicate the subject and time point to which BioSEND should link the samples.
- CSF processing kits are ordered independently of blood kits, as CSF is not required
- All specimen labels (including CSF) will be included in the Blood Collection Kit. If CSF is not collected at a visit, you may discard these extra labels

Kit Type **Please allow two weeks for shipment** * must provide value	<div><input checked="" type="radio"/> Baseline/Annual Visit Kit</div> <div><input type="radio"/> CSF Collection Kit</div> <div><input type="radio"/> Extra Supplies</div>
Please specify in comments if you need kits before the standard two week shipment time.	
Baseline/Annual Visit Kit Quantity * must provide value	<input type="text" value="1"/>
Comments	<div><div></div><div>Expand</div></div>

Kit Contents and Ordering: Kit Breakdown

LBD Kit Request Module

Comments

Expand

Baseline/Annual Visit Collection Kit

15 - Siliconized cryogenic vial, 2ml

2 - Serum (glass) tube, 10ml

2 - EDTA (glass) tube, 10ml

1 - EDTA (plastic) tube, 3ml

2 - PAXGene® tube, 2.5ml

7 - Bubble-tube sleeve

2 - Disposable pipet, 3ml

1 - Cryobox, 25 cell

2 - Biohazard bag w/ absorbent sheet

1 - Fragile label

1 - UN3373 label

1 - Dry ice label

1 - Airway bill envelope

1 - Frozen shipper

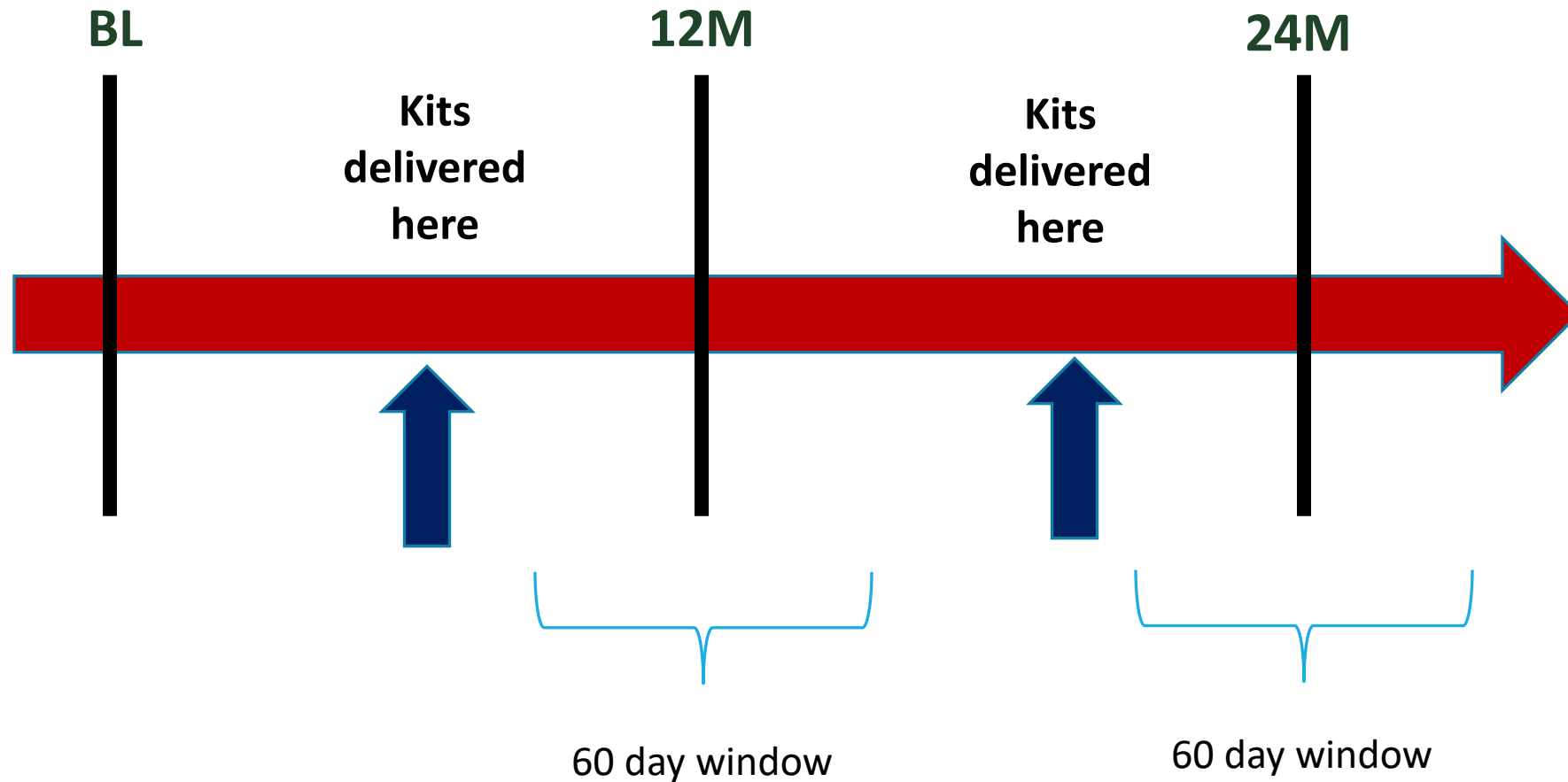
1 - Label set (kit & specimen labels)

Kit contents of selected kit will appear at the bottom of the page

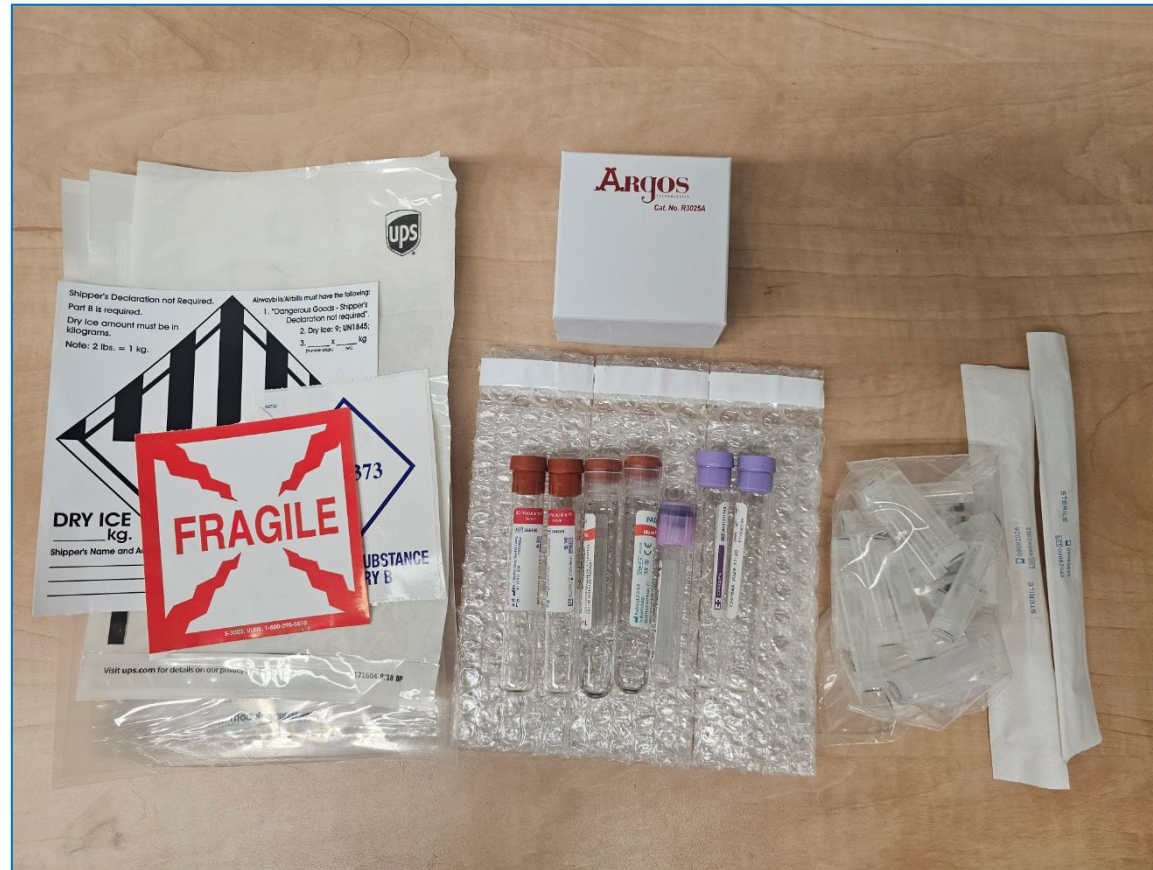
Automatic Kit Shipments

- After subject completes baseline visit and BioSEND receives BL samples, BioSEND sets up automated kit sending schedule for subject's subsequent visits
- Schedule gives 2 month window around the longitudinal study visit target (1 month on either side)
- BioSEND will send kits prior to start of study window
 - Reduces effort for study coordinators
 - Sites only need to order kits if visit will occur AHEAD of the study visit window
- All study visit target dates are determined from Baseline Visit (not from last study visit date)

Automatic Kit Shipments

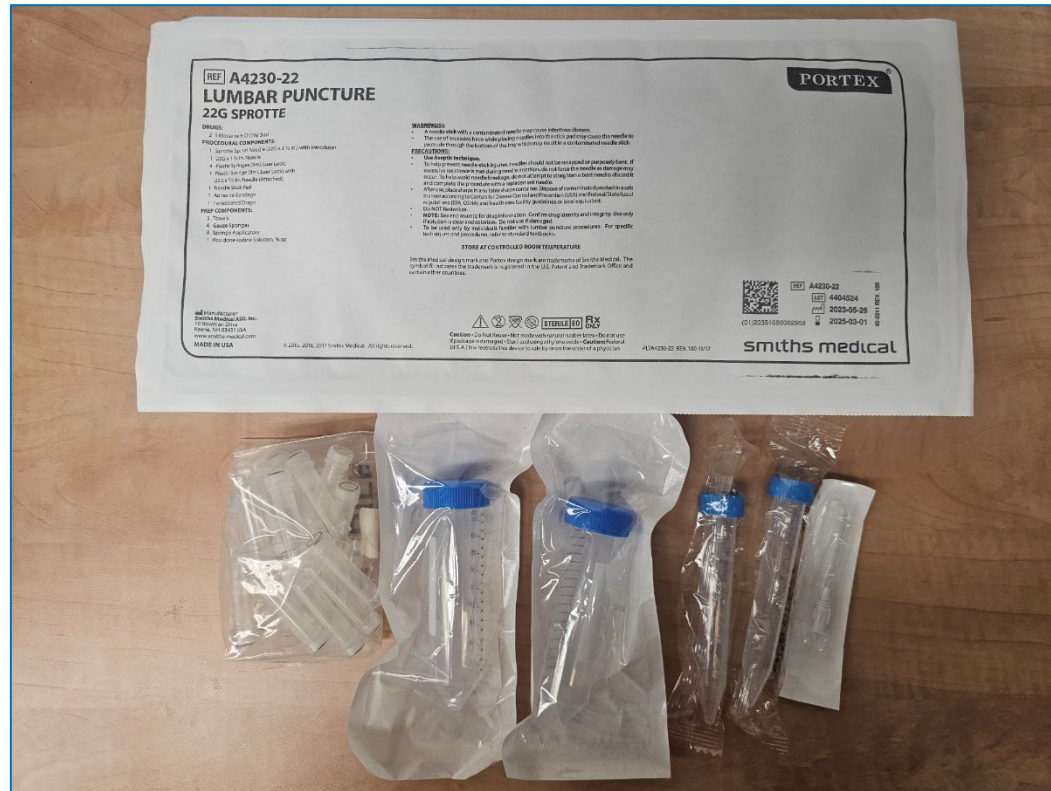


Kit Contents and Ordering: Blood Kits



Kit Contents and Ordering: CSF Kits

CSF:



LP Tray:



Collection Volumes

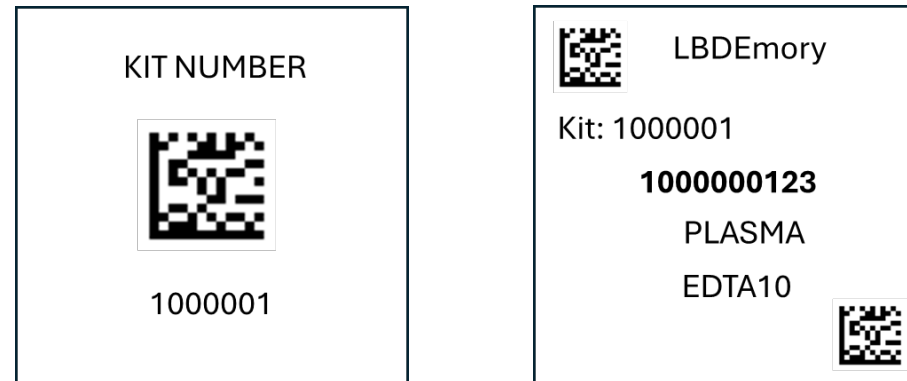
Total blood and CSF volumes

Sample Type	Amount
Whole Blood for RNA	5 ml
Whole Blood for Plasma and Buffy Coat	20 ml
Whole Blood for Serum	20 ml
Whole Blood for Banking	3 ml
Cerebrospinal Fluid	10 ml

Sample Labelling: Example Labels

Labels are provided by Indiana University

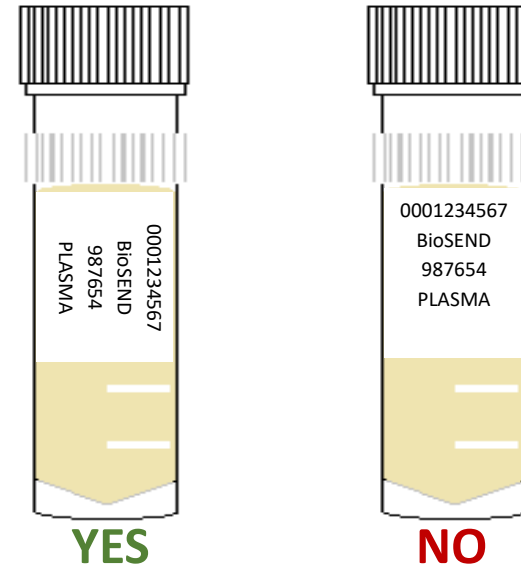
- Please check that all samples are properly labelled to ensure correct identification by IU
- If do not have enough labels to complete a visit, please contact IU *immediately*
- Labelling the tubes during processing prevents sample mix-ups



Sample Labelling: Label Placement

Please...

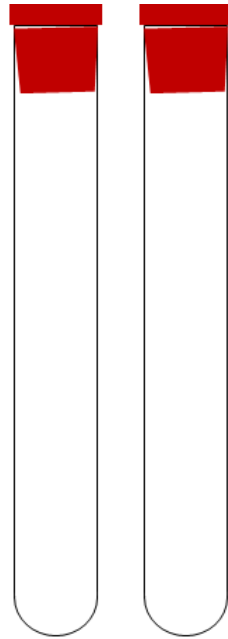
- Label all collection and aliquot tubes before cooling, collecting, processing, or freezing samples
- Label only 1 subject's tubes at a time to avoid mix-ups
- Wrap the label around the tube horizontally - label position is important for all tube types
- Make sure the label is completely adhered by rolling between your fingers



Sample Collection and Processing

Blood Tube Draw Order

2 x 10ml Serum Tubes



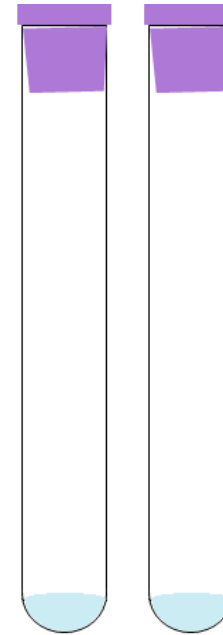
1

2 x 2,5ml PAXGene® Tubes



2

2 x 10ml EDTA Tubes



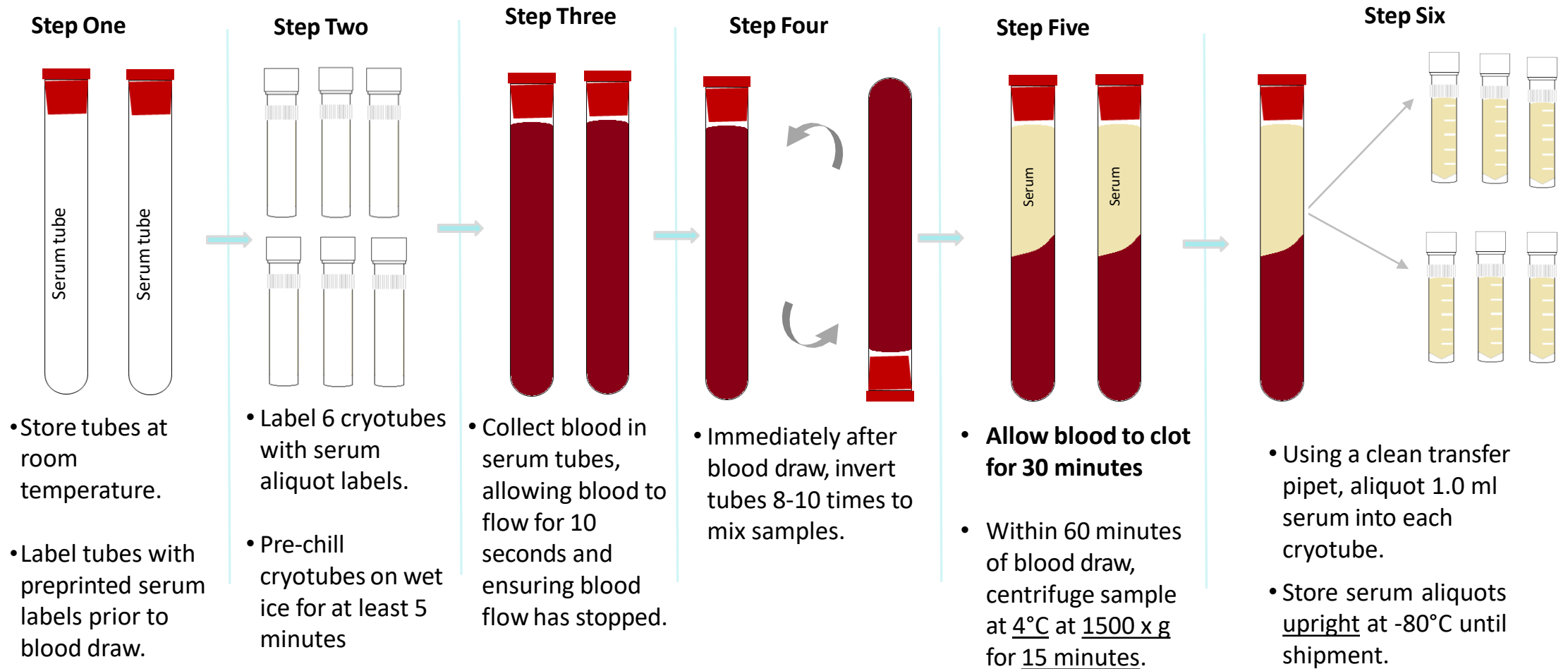
3

1 x 3ml EDTA Tube

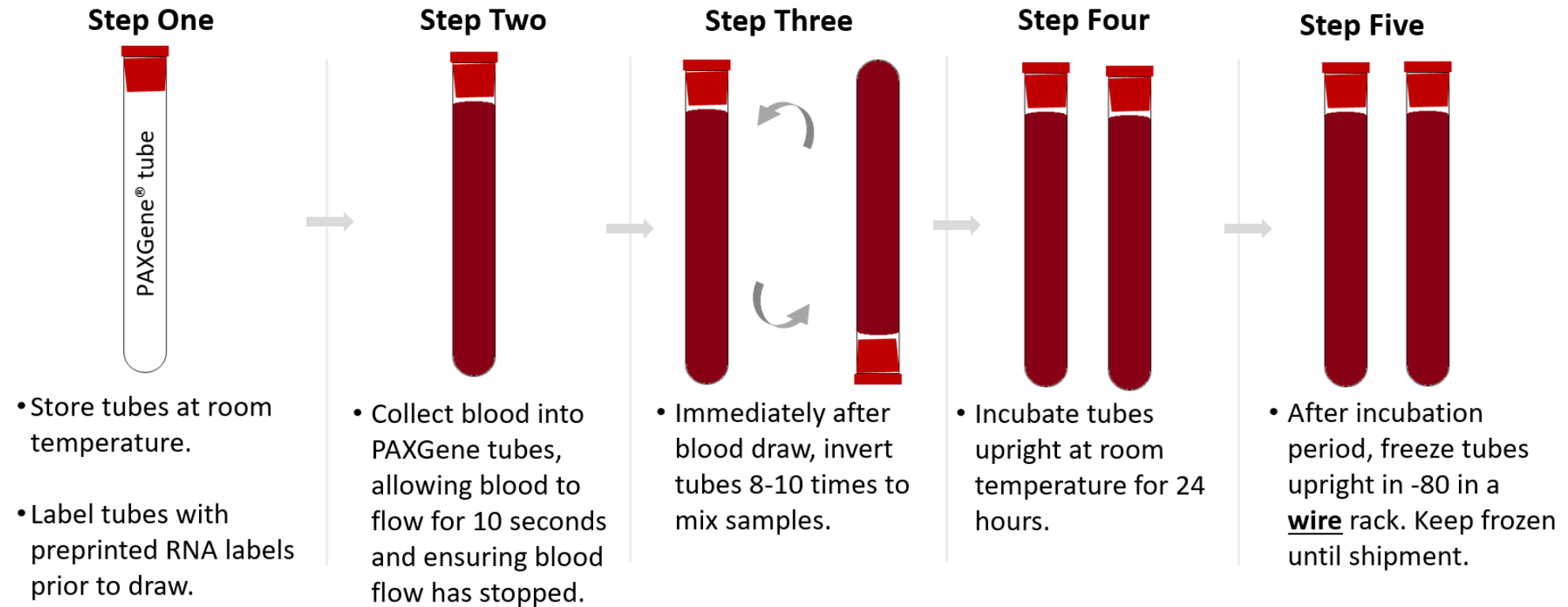


4

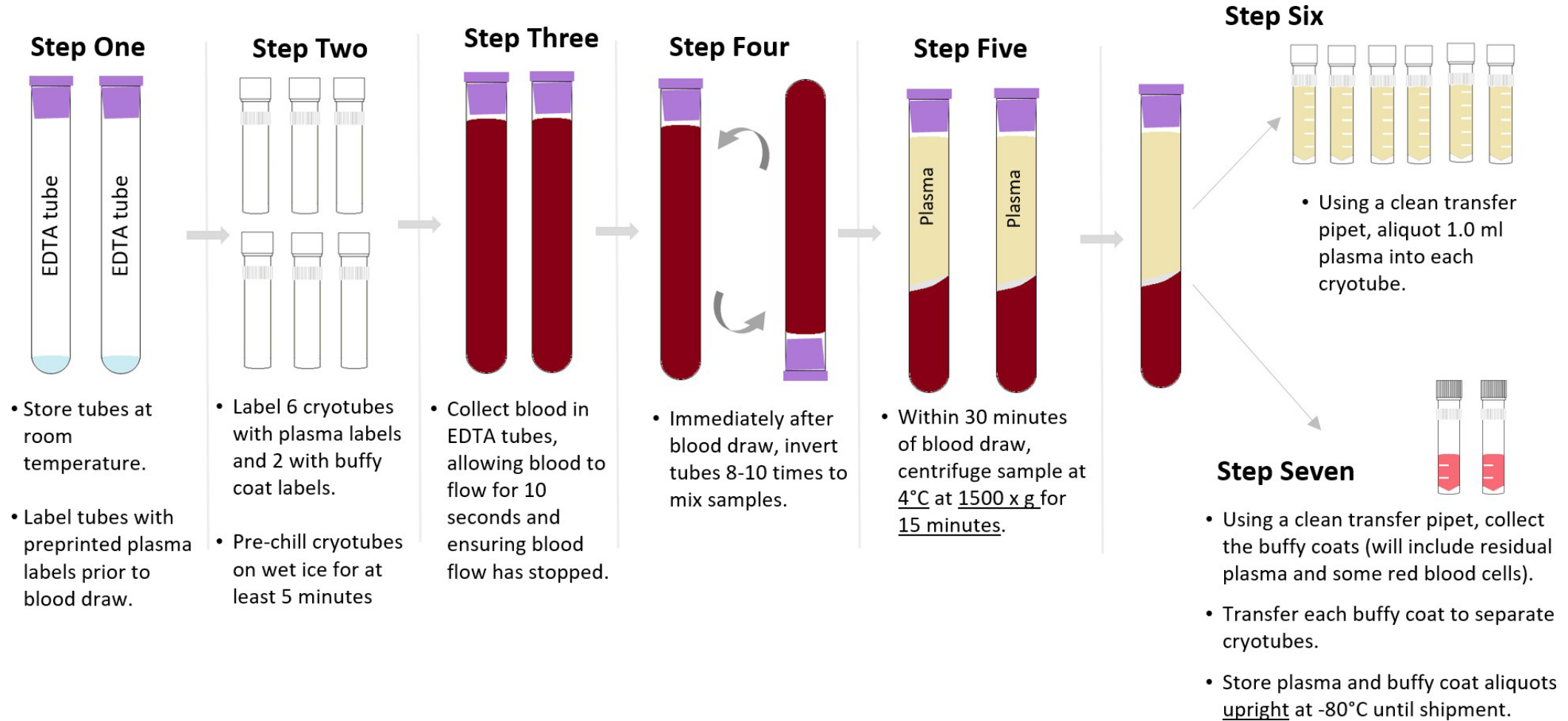
Sample Collection and Processing: Serum



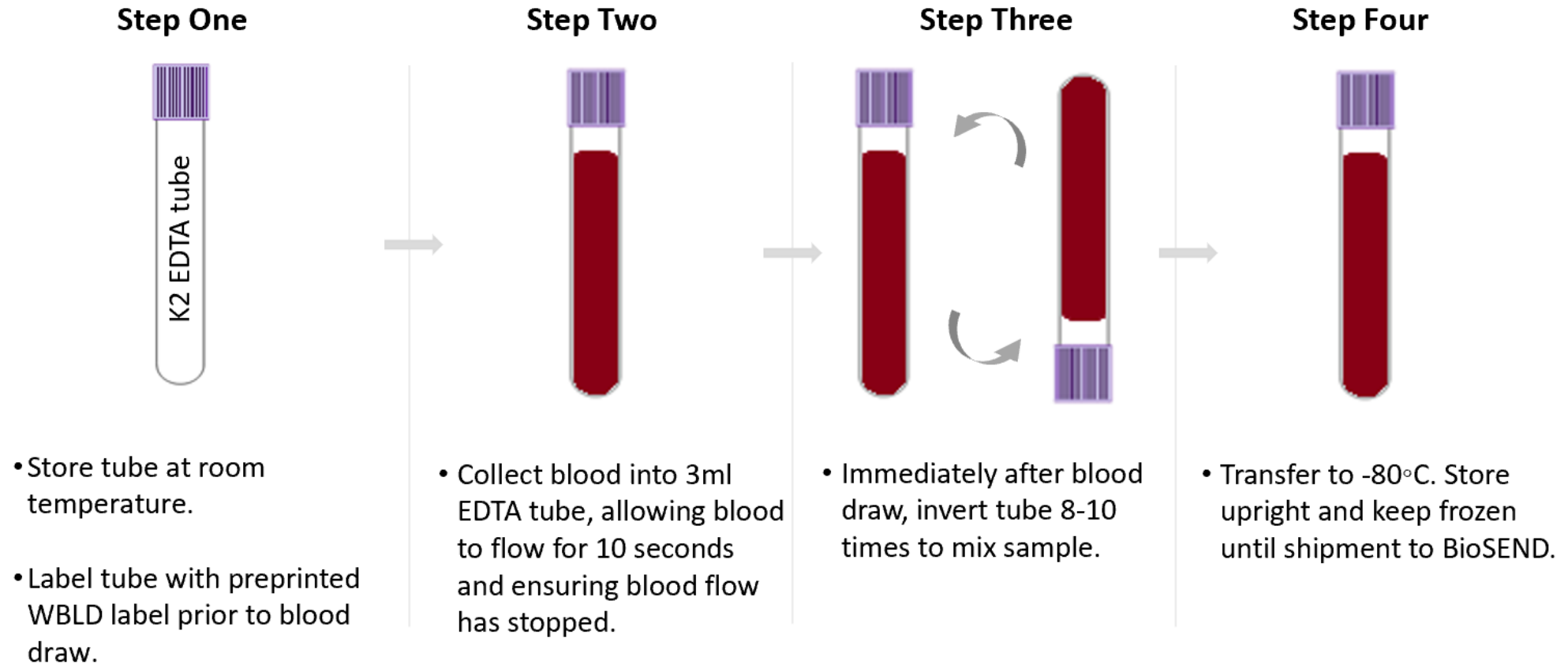
Sample Collection and Processing: Whole blood RNA



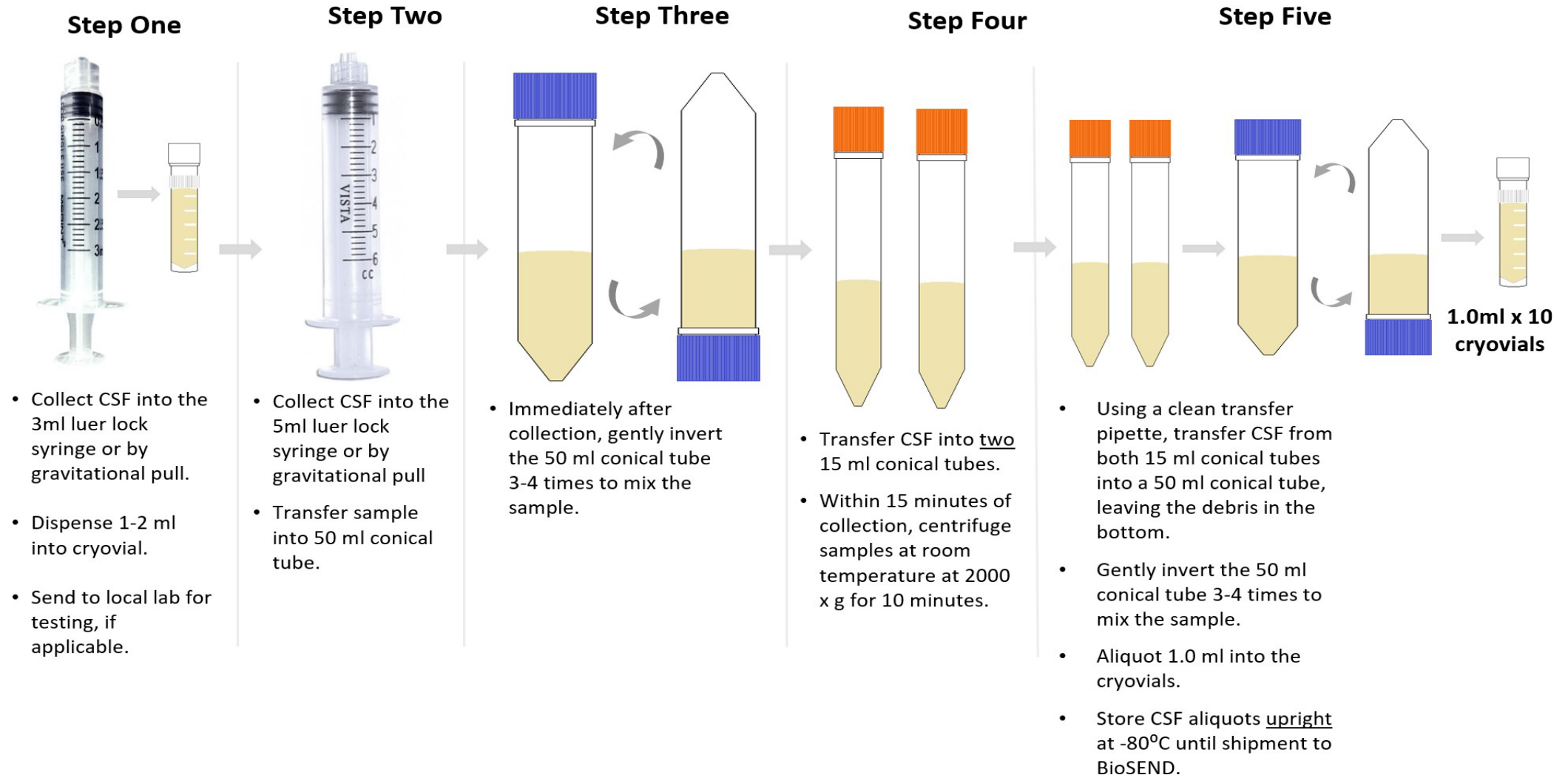
Sample Collection and Processing: Plasma & Buffy Coat



Sample Collection and Processing: Whole Blood



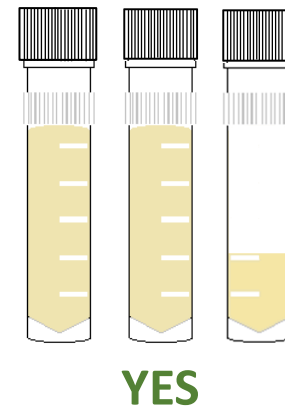
Sample Collection and Processing: CSF



Sample Collection and Processing: Aliquots

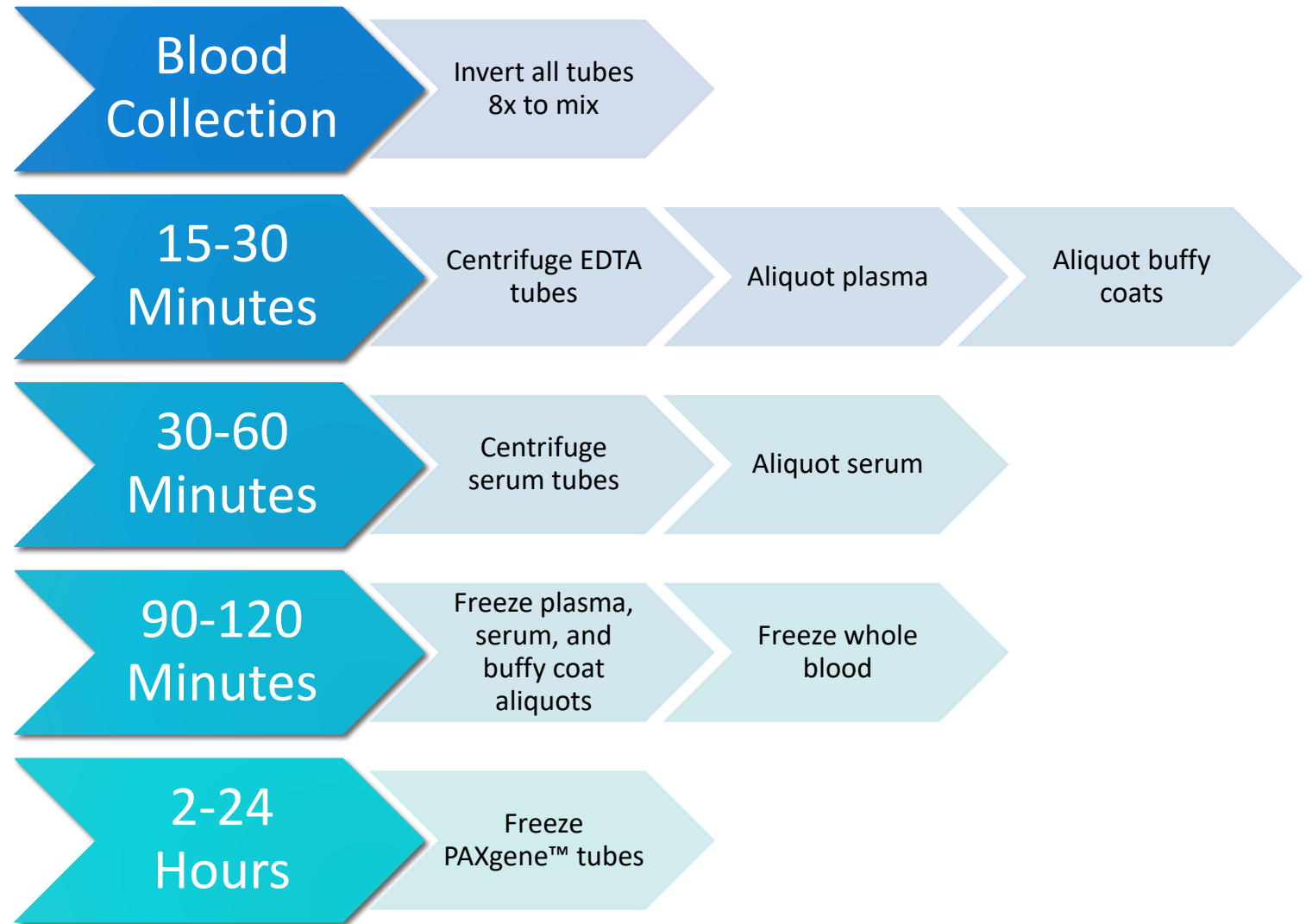
Filling biomarker serum, plasma, and CSF aliquots:

- Fill as many cryovials as possible to 1.0 ml (plasma, serum & CSF)
- Over-filled vials may burst in freezer!
- Ship ALL material to IU, even if final vial is less than standard volume



Sample Collection and Processing: Timeline

Timeline for blood processing



Sample Collection and Processing: Issue #1

Troubleshooting Blood Collection

Issue #1: Tube with little/no vacuum

- Always check expiration date on the tube before beginning blood draw and discard expired tubes
- Store tubes at “room temperature” – extreme temperature can affect vacuum
- Keep extra vacutainer tubes from supplemental kit nearby during blood draw to replace “bad” tubes
- If this is a frequent occurrence, report tube type and lot number to IU.

Sample Collection and Processing: Issue #2

Troubleshooting Blood Collection

Issue #2: Hemolyzed serum and/or plasma caused by incorrect collection

Cause: Blood Collection Methods	Corrective Action
Improper venipuncture site	Draw from median cubital, basilic, and cephalic veins from antecubital region of arm
Prolonged tourniquet use	Tourniquet should be released after no more than 1 min, excessive fist clenching should be avoided
Not allowing alcohol to dry on skin before venipuncture	Without touching, allow the venipuncture site to air dry
Use of too large/small bore needle resulting in excess force applied to blood	Avoid using too small/large needle. Needle size dependent on the subject's physical characteristics & amount of blood to be drawn. Most commonly used sizes are 19 – 23.
Pulling/pushing plunger too fast while drawing/transferring blood	Avoid drawing the syringe plunger too forcefully when collecting blood
Ensure all blood collection assemblies are fitted securely, to avoid frothing	

For more information, visit: http://www.bd.com/vacutainer/pdfs/techtalk/TechTalk_Jan2004_VS7167.pdf

Sample Collection and Processing: Issue #2 continued

Troubleshooting Blood Collection

Issue #2: Hemolyzed serum and/or plasma caused by incorrect processing

Cause: Sample Processing Methods	Corrective Actions
Vigorous mixing/shaking	Gently invert blood collection tube when mixing additive with specimen, follow guidelines in Biologics Manual regarding number of times to invert each type of tube
Not allowing serum to clot for recommended time	Serum tubes without clot activator should be allowed to clot for 60 min in a vertical position
Exposure to excessive heat or cold	Keep samples at ambient temperature until processing
Prolonged contact of serum/plasma with cells	Do not store uncentrifuged samples beyond recommended time

For more information, visit: http://www.bd.com/vacutainer/pdfs/techtalk/TechTalk_Jan2004_VS7167.pdf

Sample Collection and Processing Form

Direct link:

<http://kits.iu.edu/biosend/EmoryLBDSampleForm>

First part captures basic subject and visit information





<h1>BioSEND</h1>		Returning?
<h2>Biospecimen Exchange for Neurological Disorders</h2>		AAA + -
Please complete the Specimen Collection and Processing Form, below.		
LBD Emory Study (PDBP Study ID 238)		
Study Site	Emory University ▼	
Email address of staff member completing this form	<input type="text"/>	
<i>Note: A copy of the completed sample form and the shipping manifest will be sent to this address.</i>		
GUID	<input type="text"/>	
Sex (used for DNA quality control)	<input type="text" value="▼"/>	
Visit	<input type="text" value="▼"/>	
Kit Number	<input type="text"/>	

Sample Collection and Processing Form

Direct link:

<http://kits.iu.edu/biosend/EmoryLBDSampleForm>

Second part captures collection information

Date of venipuncture blood collection	<input type="text"/>  Today M-D-Y
Time of venipuncture blood collection	<input type="text"/>  Now H:M Use 24 Hour clock
CSF	
Was CSF collected?	<div>Yes</div> <div>No</div> <div>reset</div>
Date of CSF collection	<input type="text"/>  Today M-D-Y
Time of CSF collection	<input type="text"/>  Now H:M Use 24 Hour clock
Collection/ Processing notes	<div></div> <div>Expand</div>
<div>Submit</div>	

Sample Collection and Processing Form

Direct link:

<http://kits.iu.edu/biosend/EmoryLBDSampleForm>

PDF form of responses will be emailed to you. **Print a copy of the Frozen Shipping Manifest and include with shipment.**

LBD Emory Frozen Shipping Manifest

Page 6

Please verify/update the information below. When you click the "Submit" button below, a PDF copy of the Frozen Shipping Manifest will be emailed to you for Subject [subj_id].

Please print a copy of that document and include it in the shipping container.

Study Site: ☐ Emory University

GUID: _____

Visit: ☐ BL
☐ 12M
☐ 24M
☐ 36M
☐ 48M

Kit number: _____

Date of blood collection: _____

Date of CSF collection: _____

SERUM

Number of SERUM aliquots shipped: _____

RNA

Number of PAXGene™ tubes shipped: _____

PLASMA EDTA

Number of PLASMA EDTA aliquots shipped: _____

Number of BUFFY COAT aliquots shipped: _____

Shipping Frozen Samples: Tips

Packing and Shipping Frozen Samples

- Serum, plasma, buffy coats, CSF, whole blood and RNA all ship frozen
- Ship frozen samples on dry ice
- Frozen samples should be shipped **only** Monday through Wednesday
- Always fill carton to **top** with dry ice
- Do not pack shipment until the day of pickup



Shipping Samples

Packing and Shipping Frozen Samples

Class 9 Dry Ice Label should not be covered with other stickers and must be completed, or UPS will reject/return your package!

The image shows a Class 9 Dry Ice Label template. It features a large triangle with vertical bars inside, and a large '9' at the bottom. The label includes fields for shipper and consignee information, and a section for dry ice weight. Red arrows point to specific areas with labels: 'Net weight of dry ice in kg' points to the weight field, 'Your name & address' points to the shipper's name and address field, and 'IU information and address' points to the consignee's name and address field.

Shipper's Declaration not Required.

Dry Ice amount must be in kilograms.

Note: 2 lbs. = 1 kg.

Airwaybills / airbills must have the following:

1. Dry Ice; 9; UN 1845
2. $\frac{\text{Number}}{\text{(Number pks)}} \times \frac{\text{wt}}{\text{(wt)}} \text{ Kg}$

Net weight of dry ice in kg

Dry Ice kg.

Your name & address

Shipper's Name and Address

UN 1845

Consignee Name and Address

IU information and address

9


06426 1/01 RRD

Shipping Samples: Frozen

Packing and Shipping Frozen Samples



Shipping Samples – UPS: <https://kits.iu.edu/UPS>



INDIANA UNIVERSITY

SCHOOL OF MEDICINE

and Affiliated Biorepositories

Search for address

Code

Company

Contact

Address 1

Address 2

Address 3

City

State/Province

Postal Code

Country/Territory

Icahn School of Medicine - Mt. Sinai

Kenny Persaud

1425 Madison (Icahn Building)

Icahn L4 39

New York

NY

10029

United States

Shipment Information

Study Group

Weight

Dry Ice Weight

Description of Return

SSBC

20

10

Biologic Specimens

Pickup Request

Choose Study

Enter weight

Click "Ship"

Reset

Ship

Shipping Samples via UPS

IU UPS ShipExec Shipping Portal

- Print out UPS air waybill
- Ensure all elements (barcode, return address, etc.) printed clearly
- Fold and insert UPS air waybill into clear plastic sleeve on package

JOHN SMITH INDIANA UNIVERSITY 410 WEST 10TH STREET INDIANAPOLIS IN 46202	2 LBS	1 OF 1
RS		
SHIP TO: SCHOOL OF MEDICINE 317-278-2694 INDIANA UNIVERSITY TK 217 351 W 10TH ST INDIANAPOLIS IN 46202		
	IN 461 9-01	
		
UPS NEXT DAY AIR		1
TRACKING #: 1Z 976 R8W 84 3985 8595		
 SAMPLE		
BILLING: P/P DESC: Biological Specimens RETURN SERVICE		
Reference No.1: 4087277		
XOL 20.03.09 NV45 83.0A 12/2019		 TM

Non-Conformance

Non-conformance to standard procedures may reduce the utility of the biospecimens:

- Not processing serum/plasma within 2 hours of collection allows for breakdown of certain proteins and small molecules
- Over/under centrifuging changes plasma, serum, CSF composition



Non-Conformance Reporting con't

Most common non-conformance issues:

- Shipment notification not sent
- Samples shipped for weekend/holiday delivery
- Sample form incomplete/inaccurate
- Low volume
- Unlabeled or mislabeled tube(s)
- Sample hemolysis



BioSEND.org

On the website, you can:

- Access your study's kit request module and sample submission form
- Download the most recent version of the Manual of Procedures
- View a recording of this training
- Find information about holiday closures
- Access shipping resources

Study Resources

KIT REQUEST MODULE

Please follow the below link to access the Kit Request Module. This link will direct you to a REDCap database where study coordinators and staff may request kits, individual supplies, and/or labels. Please allow a total of two weeks for kit requests to be fulfilled.

[Kit Request System →](#)

SPECIMEN COLLECTION AND PROCESSING FORM

Please use the below link to access the collection and processing form for this protocol. This form must be completed prior to shipment. We also ask that all shipments include a physical copy of the shipping manifest portion of the form.

[Specimen Collection and Processing Form →](#)

MANUAL OF PROCEDURES

The below downloadable manual was created specifically for the DxCTEII study. Please feel free to explore the manual through the hyperlinked 'Table of Contents'. Questions concerning any part of the manual may be directed to biosend@iu.edu for further clarification.

[Manual of Procedures ↓](#)

TRAINING SLIDES

These slides correspond to the BioSEND DxCTEII protocol training. Training is available upon request by contacting biosend@iu.edu.

[Training Slides ↓](#)

SAMPLE SHIPPING

BioSEND can receive samples Monday-Friday, excluding holidays. Frozen samples should be shipped M-W. Ambient samples may be shipped on Th.

[Generate UPS airbill or schedule pickup →](#)
[Check holiday closures →](#)
[What do I do for Friday blood draws →](#)

Contacts

Indiana University

General Questions/Shipment Notifications:

biosend@iu.edu

317-278-6158

Request kits:

<http://kits.iu.edu/biosend/EmoryLBD>