



Biospecimen Exchange for Neurological Disorders

An Intermediate-Size Expanded Access Protocol for Amyotrophic Lateral Sclerosis with Pridopidine (Pridopidine EAP2)

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

Collection Tube	Drawn At	Specimen Type	Aliquot Volume	Total Number of Aliquots/Tubes Shipped to BioSEND	Cryovial Cap Color
2 EDTA (plastic) Blood Collection Tubes, 10ml	BL, Week 12, Week 52, Week 104	Plasma	1.5ml	6	Purple
	BL, Week 12, Week 52, Week 104	Buffy Coat	~500-750ul	2	Clear

*If participant does not consent to DNA collection and banking, buffy coat specimens should not be collected. Please see Appendix B for details.

Kit Contents and Ordering

- All sites will be sent a Supplemental Kit with their first kit shipment
 - Contains extra blood collection tubes and processing supplies
 - 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

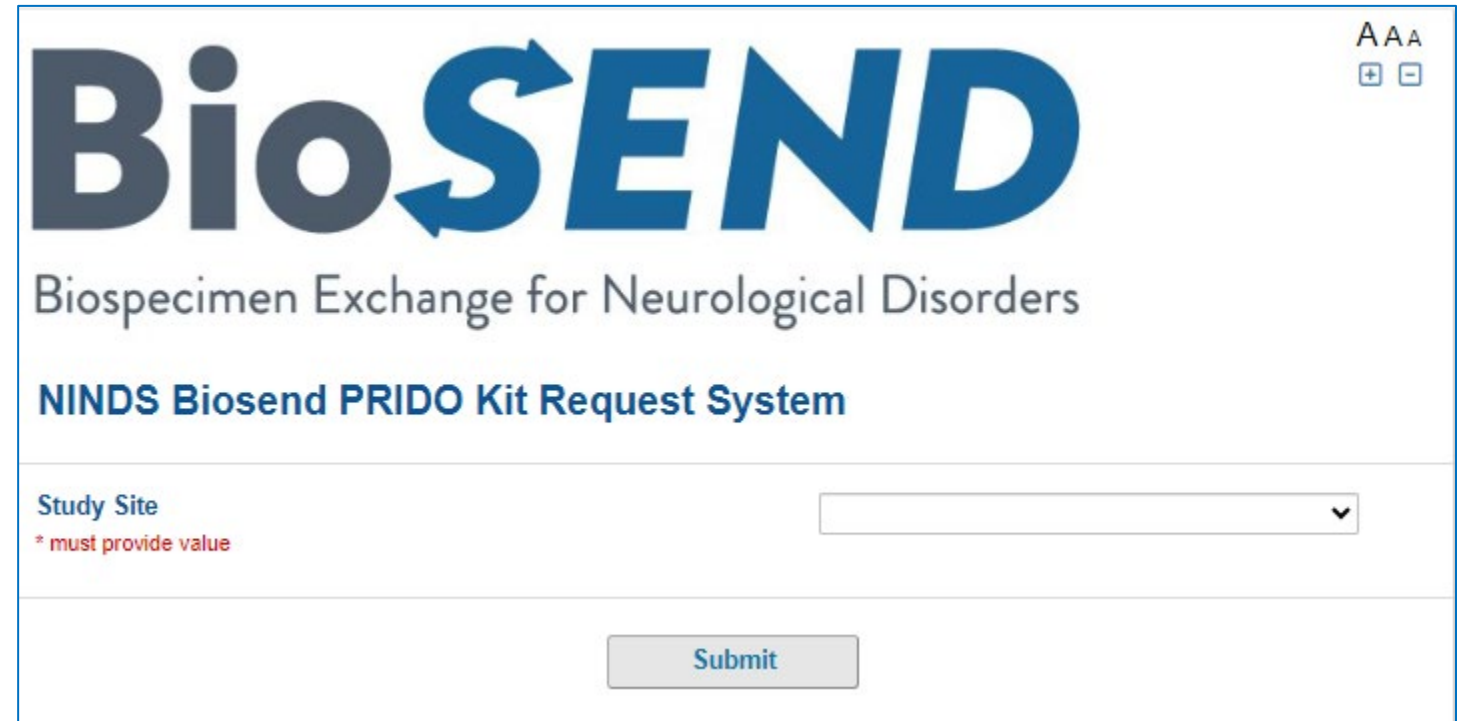
Kit Contents and Ordering – REDCap Survey

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

Order kits online through the Kit Request Module for:

- Blood kits
- Shipping kits
- Extra Supplies

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



The screenshot shows the 'Biosend' logo in large blue letters, with 'Bio' in a standard font and 'SEND' in a bold, italicized font. Below the logo is the text 'Biospecimen Exchange for Neurological Disorders'. Underneath that is the title 'NINDS Biosend PRIDO Kit Request System'. There is a dropdown menu labeled 'Study Site' with a red asterisk and the text '* must provide value' below it. A 'Submit' button is located at the bottom right of the form area. In the top right corner of the interface, there are three small icons: 'A A A' and two square buttons with plus and minus signs.

Kit Contents and Ordering: Confirm Site Info

PRIDO Kit Request Module

Study Site <small>* must provide value</small>	<input type="text" value="Indiana University"/>	<div>Select your site from the drop-down list</div>
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		
Is the contact name above correct? <small>* must provide value</small>		<div><input type="radio"/> Yes <input checked="" type="radio"/> No</div> <div>reset</div>
New Contact Name <small>* must provide value</small>		<input type="text" value="Claire Wegel"/>
Is the shipping address above correct? <small>* must provide value</small>		<div><input type="radio"/> Yes <input type="radio"/> No</div> <div>reset</div>
Is the e-mail address above correct? <small>* must provide value</small>		<div><input type="radio"/> Yes <input type="radio"/> No</div> <div>reset</div>
Is the phone number above correct? <small>* must provide value</small>		<div><input type="radio"/> Yes <input type="radio"/> No</div> <div>reset</div>

Kit Contents and Ordering: Kit Types

PRIDO 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.
- Standard collection kit for plasma and buffy coat contains supplies for one subject-visit.
- Shipping Kits are ordered independently of Blood Kits
- A single Shipping Kit may be used to send samples for 1-2 cryoboxes

Kit Type **Please allow two weeks for shipment** * must provide value	<div><input checked="" type="radio"/> Blood Collection Kit</div> <div><input type="radio"/> Shipping Kit</div> <div><input type="radio"/> Extra Supplies</div>
Please specify in comments if you need kits before the standard two week shipment time.	
Blood Collection Kit Quantity * must provide value	<input type="text" value="3"/>
Comments	<div><div></div><div>Expand</div></div>

Kit Contents and Ordering: Kit Breakdown

PRIDO Kit Request Module

Comments

Expand

Each Blood Collection Kit contains:

2 - EDTA tube, 10ml (plastic)

6 - Cryovial (Sarstedt®) with purple cap, 2ml

2 - Cryovial (Sarstedt®) with clear cap, 2ml

2 - Disposable pipette, 3ml

2 - Resealable tube pouch

1 - Cryobox, 25 slot

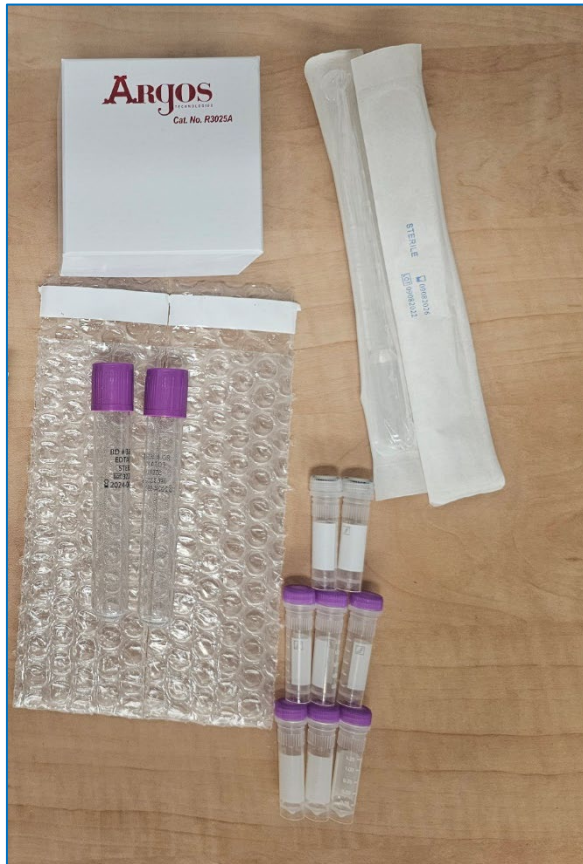
1 - Specimen/Case label set-- Kit numbers

Submit

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

Kit Contents and Ordering: Kits

Blood Kit (frozen):



Shipping Kit:



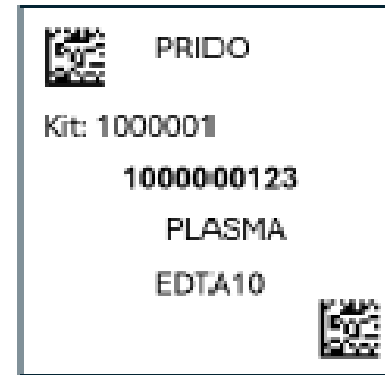
Kit and Supply Ordering

- Click “Submit” to send order to BioSEND; staff will confirm receipt of your order
- Please allow two week turn-around time for kit shipments
- If urgent request needed, please note date needed by in comments and email BioSEND. We cannot guarantee urgent orders, but we will do our best to accommodate.
- BioSEND will send confirmation of shipment and tracking number when supplies ship

Sample Labelling: Example Labels

Labels are provided by Indiana University

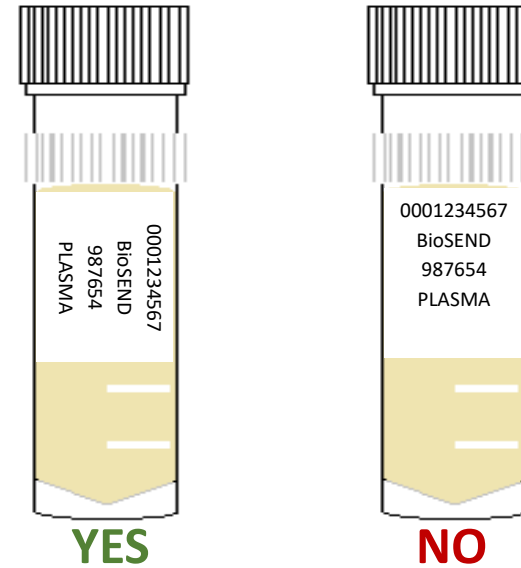
- Please check that all samples are properly labelled to ensure correct identification by IU
- If do not have enough labels to complete a visit, please contact IU *immediately*
- Labelling the tubes during processing prevents sample mix-ups



Sample Labelling: Label Placement

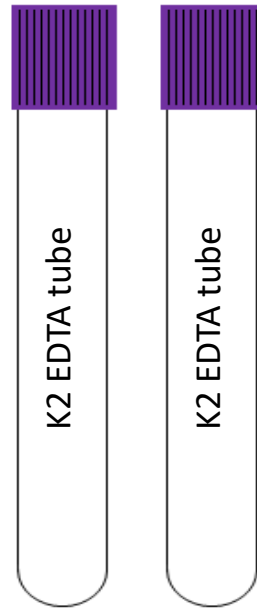
Please...

- 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

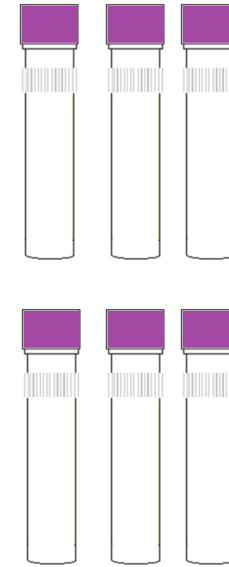


Sample Collection and Processing

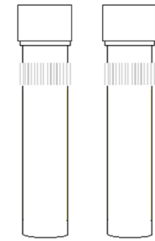
Supplies provided for the collection of plasma and buffy coat



2 x 10ml EDTA
(plastic) collection
tubes

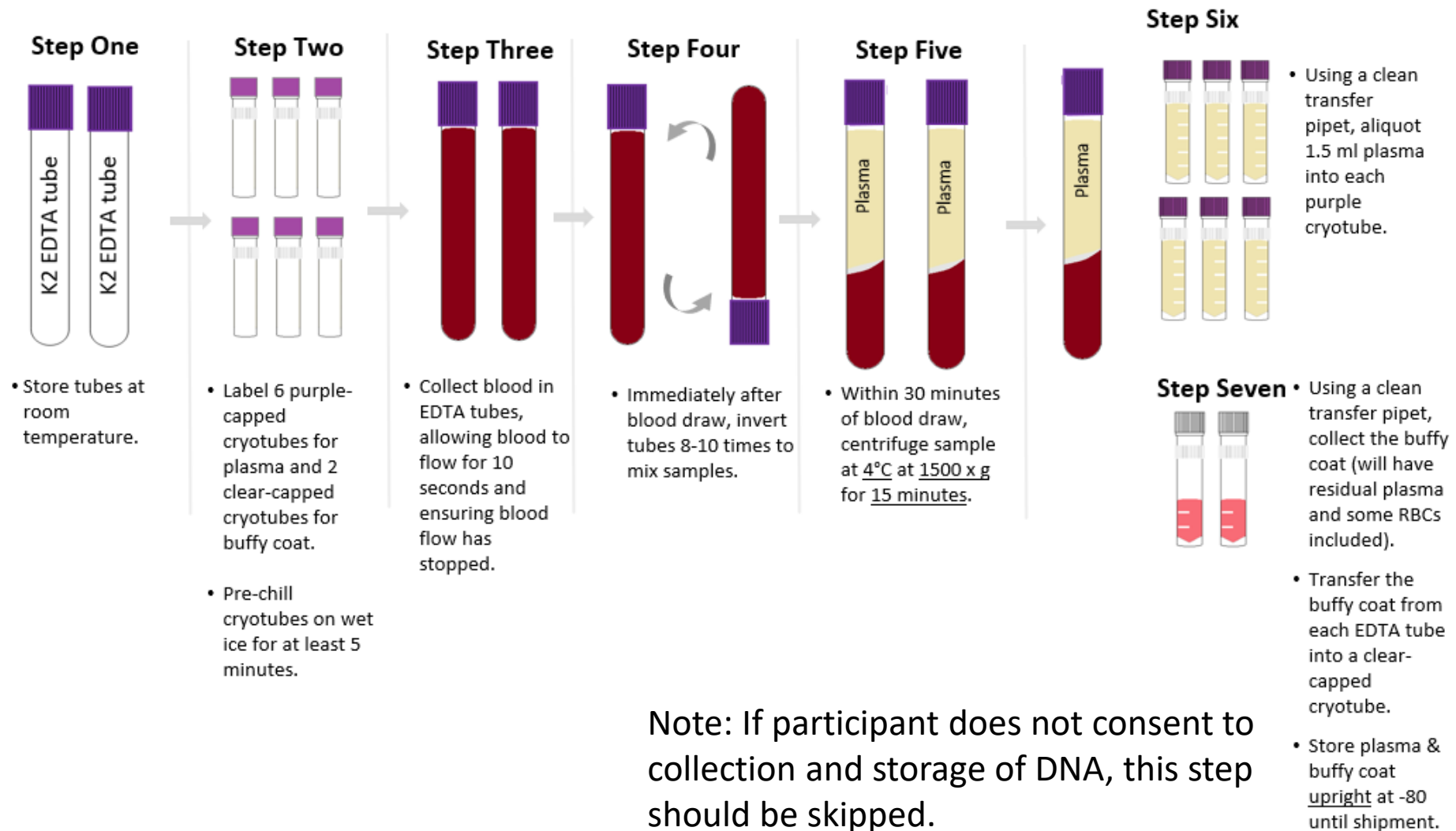


6 x 2ml Cryovials
(purple-capped) for
plasma aliquots



2 x 2ml Cryovials
(clear-capped) for
buffy coat aliquots

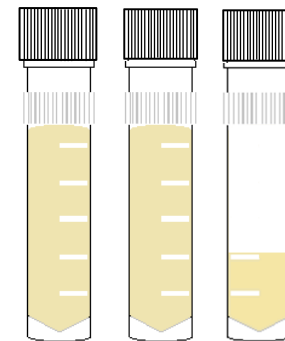
Sample Collection and Processing: Plasma & Buffy Coat



Sample Collection and Processing: Aliquots

Filling biomarker plasma aliquots:

- Fill as many cryovials as possible to 1.5 ml (plasma)
- Over-filled vials may burst in freezer!
- Ship ALL material to IU, even if final vial is less than standard volume



YES



NO

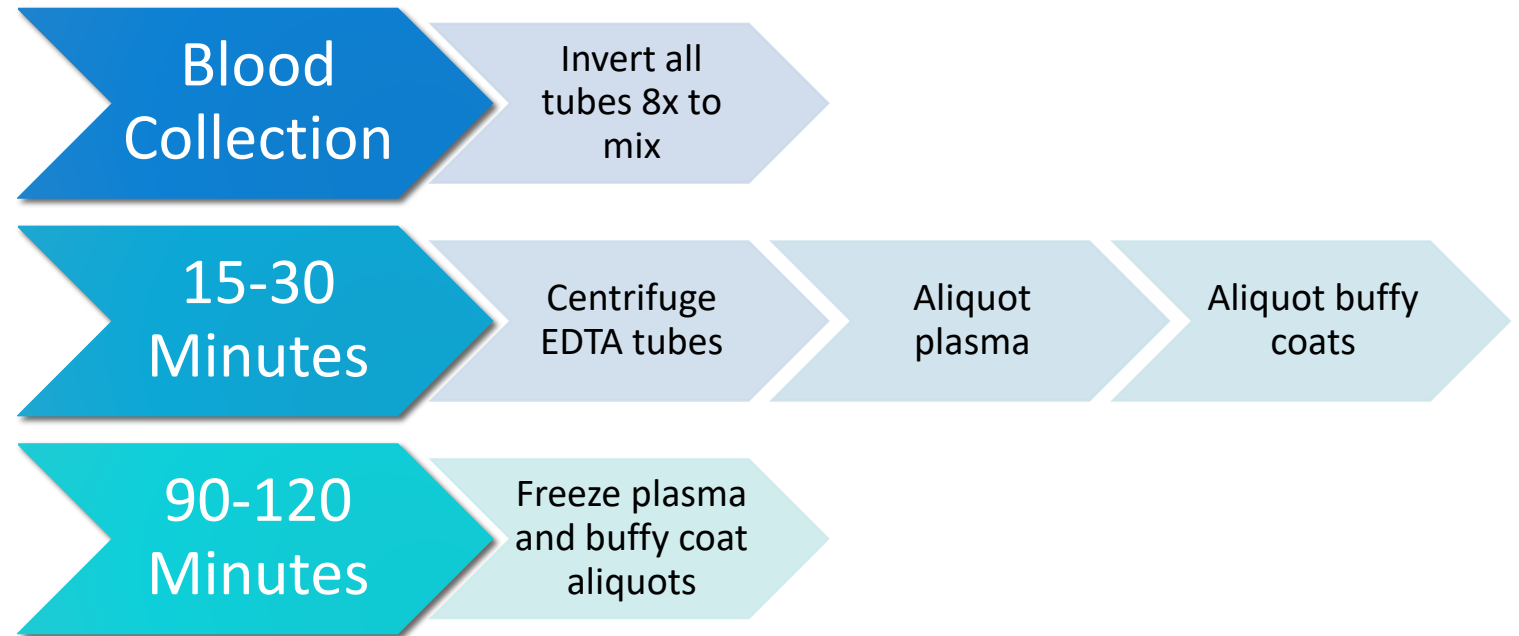
Collection Volumes

Total blood volumes

Sample Type	Amount
Whole Blood for Plasma and Buffy Coat	20 ml

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, basalic, 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

Specimen Collection and Processing Form

Direct Link:

<https://kits.iu.edu/biosend/PRIDOSampleForm>

First page captures basic subject and visit information

NINDS
BIOSEND

[Returning?](#)
AAA
+ -

Please complete the Specimen Collection and Processing Form, below.

Protocol: An Intermediate-Size Expanded Access Protocol for Amyotrophic Lateral Sclerosis with Pridopidine (Pridopidine EAP2)

Page 1 of 2

Study	PRIDO ▾
Study Site	▾
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>	
Clinical ID:	<input type="text"/>
Sex (used for DNA quality control)	▾
Did participant consent to the collection and storage of DNA?	<div>Yes</div> <div>No</div> <div>reset</div>
Visit	▾
IU Kit Number	<input type="text"/> 6 characters remaining

Sample Collection and Processing Form


Second page captures processing information

Blood Collection and Processing

Date of venipuncture blood collection

 Today M-D-Y

Time of venipuncture blood collection

 Now H:M
Use 24 Hour clock

Date participant last ate

 Today M-D-Y

Time participant last ate

 Now H:M

2. PLASMA and BUFFY COAT (Purple-top EDTA tubes, 10 mL)


Was blood collected and processed for PLASMA EDTA?

Yes

No

reset

Time of PLASMA EDTA tube centrifugation

 Now H:M
Use 24 Hour clock

Duration of PLASMA EDTA tube centrifugation

minutes

Rate of PLASMA EDTA tube centrifugation

x g

Sample Collection and Processing Form

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

PRIDO 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 Kit #[kit_num] shipping container.

Study ☐ PRIDO

Study Site: ☐ Massachusetts General Hospital

Clinical ID: _____

Visit: ☐ Baseline
☐ 12 Week
☐ 52 Week
☐ 104 Week

IU Kit Number: _____

Date of blood collection: _____

PLASMA EDTA

Number of PLASMA EDTA aliquots shipped: _____

Number of BUFFY COAT aliquots shipped: _____

Shipping Information - Please complete.

Frozen shipments should be sent Monday-Wednesday only. Please check for holiday closures prior to shipping. Contact us at biosend@iu.edu if you are unsure whether or not it is safe to ship.

Date of shipment: _____

Did/will you use the IU UPS interface to generate the shipping label? ☐ Yes
☐ No

Which shipping service did you use? ☐ UPS
☐ FedEx
☐ World Courier
☐ Other

What is the shipment tracking number? _____

Sample Collection and Processing Form

Submission of the Shipping Manifest portion of the form serves as shipment notification to BioSEND

- Must be completed prior to shipment
- If samples are shipped and not received, BioSEND will follow-up with courier. It is recommended that sites also track shipment to ensure safe delivery

Shipping Frozen Samples: Tips

Packing and Shipping Frozen Samples

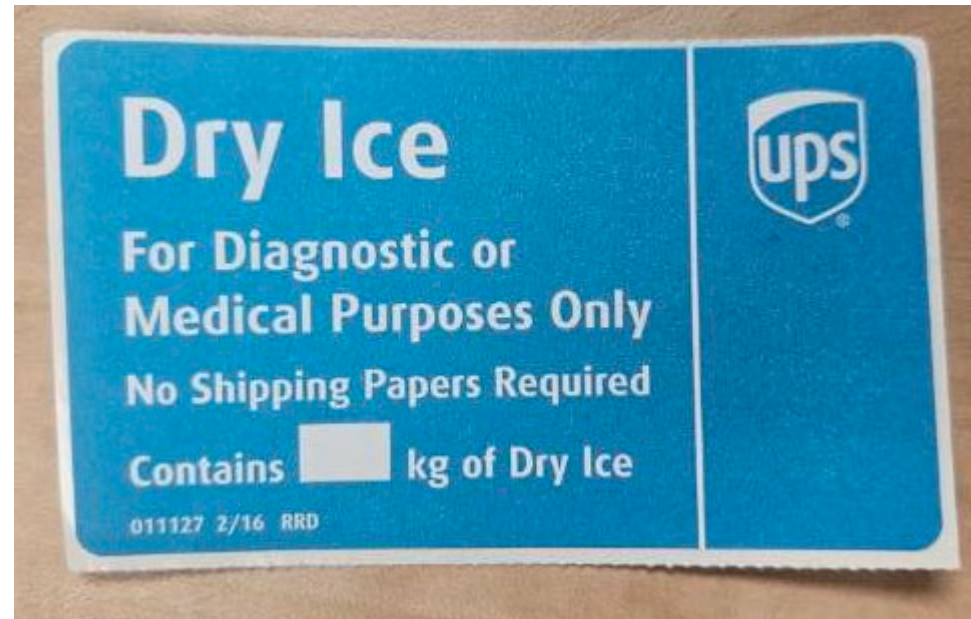
- All PRIDO samples ship frozen
- Ship frozen samples on dry ice
- Frozen samples should be shipped **only** Monday through Wednesday
- Always fill carton to **top** with dry ice
- Do not pack shipment until the day of pickup



Shipping Samples

Packing and Shipping Frozen
Samples

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



Shipping Samples: Frozen

Do not ship more than 4 biohazard bags in a single shipper (equivalent to four subject-visits).

- Allows room for dry ice to keep samples frozen in transit
- Minimizes loss in the rare but unfortunate event of courier issues



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

The screenshot shows the 'Ship From' and 'Shipment Information' sections of the IU School of Medicine shipping form. Annotations include:

- Search for address:** Points to the search icon in the 'Ship From' section.
- Schedule Pickup:** Points to the 'Pickup Request' button.
- Choose Study:** Points to the 'Study Group' dropdown menu.
- Enter weight:** Points to the 'Weight' and 'Dry Ice Weight' input fields.
- Click "Ship":** Points to the 'Ship' button at the bottom right.

The form contains the following data:

Ship From	
Code	
Company	Icahn School of Medicine - Mt. Sinai
Contact	Kenny Persaud
Address 1	1425 Madison (Icahn Building)
Address 2	Icahn L4 39
Address 3	
City	New York
State/Province	NY
Postal Code	10029
Country/Territory	United States

Shipment Information	
Study Group	SSBC
Weight	20 LB
Dry Ice Weight	10 LB
Description of Return	Biological Specimens

Buttons: Clear, Pickup Request, 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

Shipping Samples: Closures

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	Juneteenth (observed)
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

Please also consider weather when shipping. UPS will post service updates on their webpage. Reach out to BioSEND if you are unsure if it is safe to ship.

Non-Conformance

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

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



Non-Conformance and Inventory Reporting

Most common non-conformance issues:

- BioSEND will notify sites directly of any issues upon receipt
- BioSEND will email sites a monthly inventory report of all samples received from that site to date
- ***If you are experiencing issues, please reach out to us for help! It is much easier to prevent an issue before sample collection & shipment than trying to fix it after the fact***

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/prido>