



Biospecimen Exchange for Neurological Disorders

Risk and Resilience, Clinical presentation, and Biomarker  
Profiles of Chronic Traumatic Encephalopathy and Related  
Dementias: The DIAGNOSE CTE Research Project II

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BIOSPECIMEN COLLECTION & PROCESSING

# Overview

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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

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GENERAL REMINDERS



# Specimen Standardization and Quality

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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](mailto:biosend@iu.edu)

# Site Consumables and Equipment

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*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

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MAINTAINING SPECIMEN UNIFORMITY AND QUALITY

# Biospecimen Collection Protocol

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Collection Tube	Drawn At	Specimen Type	Aliquot Volume	Total Number of Aliquots	Cryovial Cap Color	Shipping Temperature
2 EDTA (plastic) Blood Collection Tubes, 10ml	BL	Plasma	1.5ml	6	Purple	Frozen
	BL	Buffy Coat	~750ul	2	Clear	Frozen
2 SERUM (plastic) Blood Collection Tubes, 10ml	BL	Serum	1.5ml	6	Red	Frozen

# Kit Contents and Ordering

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- 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



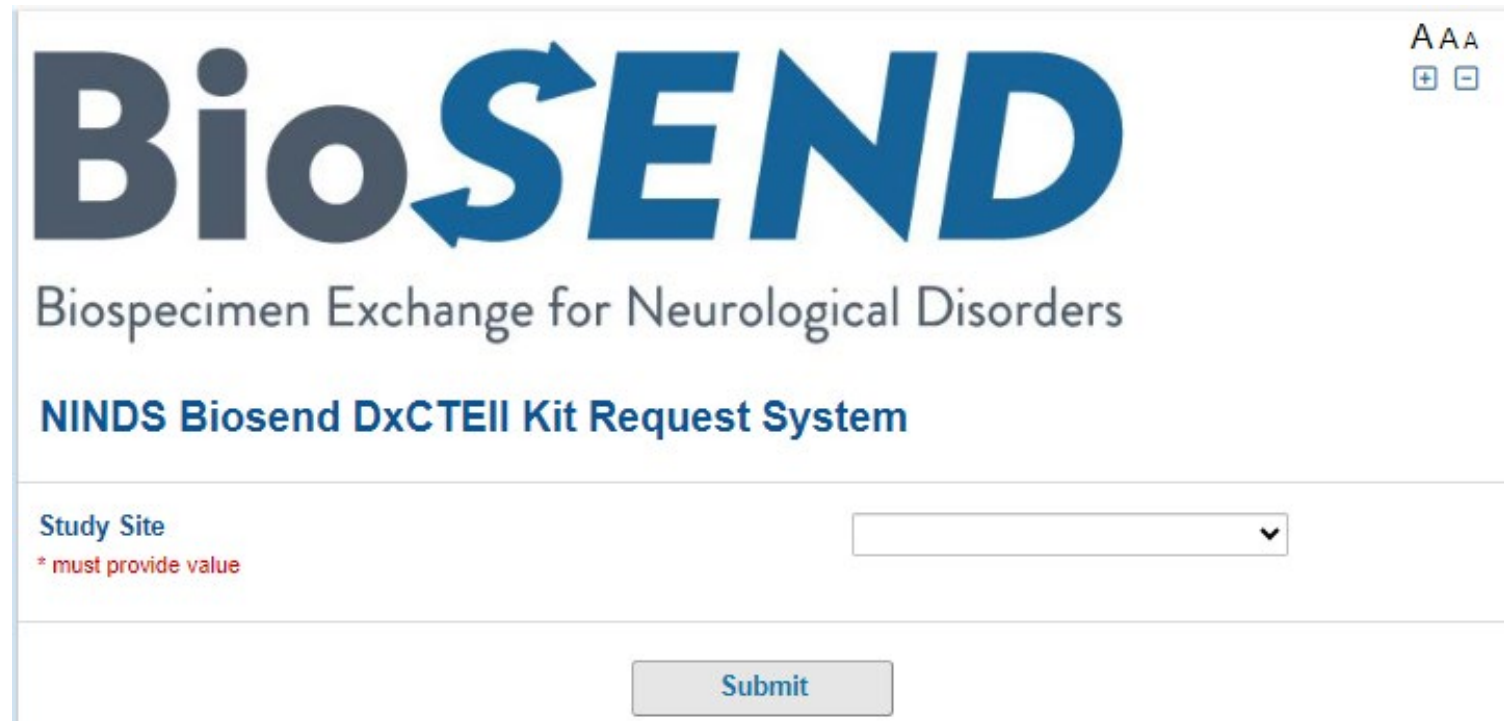
# Kit Contents and Ordering – REDCap Survey

<https://redcap.link/dxctellkits>

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 the 'S' containing a circular arrow. Below the logo is the text 'Biospecimen Exchange for Neurological Disorders' and 'NINDS Biosend DxCTEII Kit Request System'. A form field for 'Study Site' is present, with a dropdown arrow and a red asterisk warning '\* must provide value'. A 'Submit' button is located at the bottom right of the form area. In the top right corner of the page, there are accessibility icons for font size (AAA) and a plus/minus sign.

# Kit Contents and Ordering: Confirm Site Info

DxCTEII Kit Request Module

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

# Kit Contents and Ordering: Kit Types


## DxCTEII 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, buffy coat and serum 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


<b>Kit Type</b> <b>**Please allow two weeks for shipment**</b> <i>* must provide value</i>	<input checked="" type="radio"/> <b>Blood Collection Kit</b>
	<input type="radio"/> Shipping Kit
	<input type="radio"/> Extra Supplies
	Please specify in comments if you need kits before the standard two week shipment time.
<b>Blood Collection Kit Quantity</b> <i>* must provide value</i>	<input type="text" value="3"/>
<b>Comments</b>	<div style="border: 1px solid #ccc; height: 100px; width: 100%;"></div> <p style="text-align: right; font-size: small;">Expand</p>

# Kit Contents and Ordering: Kit Breakdown

DxCTEII Kit Request Module

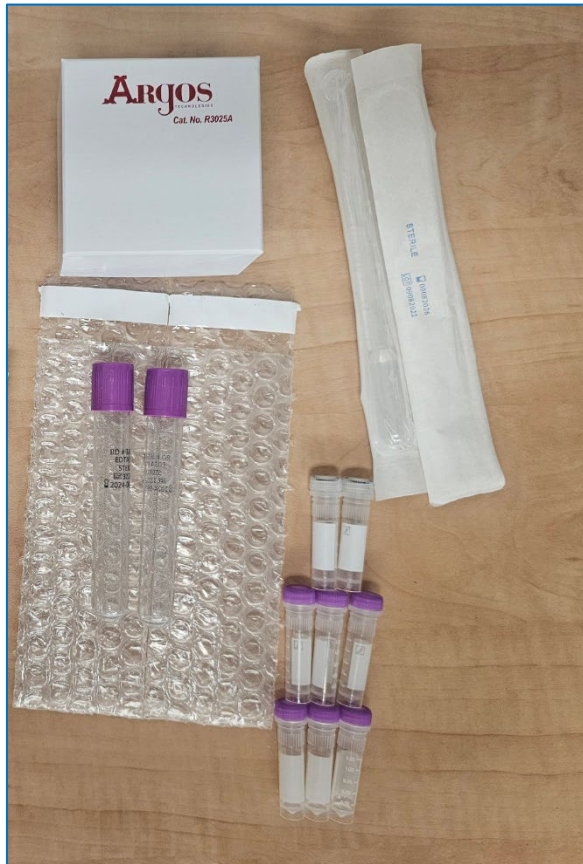
<b>Comments</b>	 <small>Expand</small>
<p><b>Each Blood Collection Kit contains:</b></p> <ul style="list-style-type: none"><li>2 - EDTA tube, 10ml (plastic)</li><li>2 - Serum tube, 10ml (plastic)</li><li>6 - Cryovial (Sarstedt®) with purple cap, 2ml</li><li>6 - Cryovial (Sarstedt®) with red cap, 2ml</li><li>2 - Cryovial (Sarstedt®) with clear cap, 2ml</li><li>2 - Disposable pipette, 3ml</li><li>2 - Resealable tube pouch</li><li>1 - Cryobox, 25 slot</li><li>1 - Specimen/Case label set-- Kit numbers</li></ul>	

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



# Kit Contents and Ordering: Kits

Blood Kit (frozen):



Shipping Kit:



# Collection Volumes

Total blood volumes

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

# Kit and Supply Ordering

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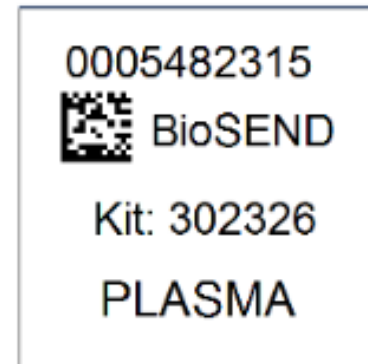
- Click “Submit” to send order to BioSEND; staff will confirm receipt of your order
- Please allow two week turn-around time for kit shipments
- If urgent request needed, please note date needed by in comments and email BioSEND. We cannot guarantee urgent orders, but we will do our best to accommodate.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

# Sample Labelling: Example Labels

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## 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



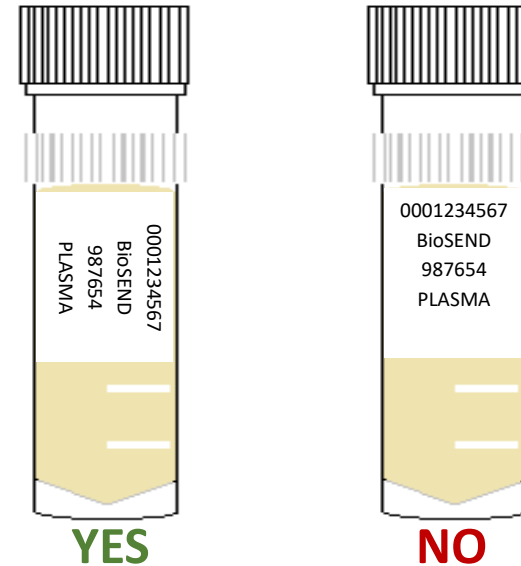


# Sample Labelling: Label Placement

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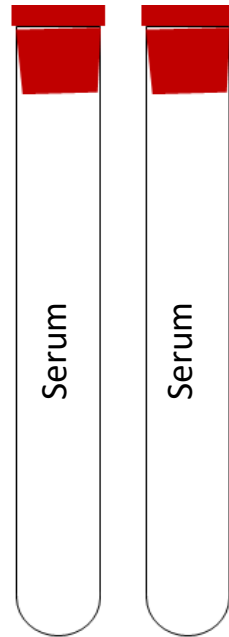
Please...

- 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

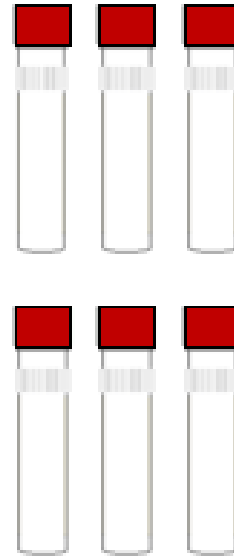


# Sample Collection and Processing

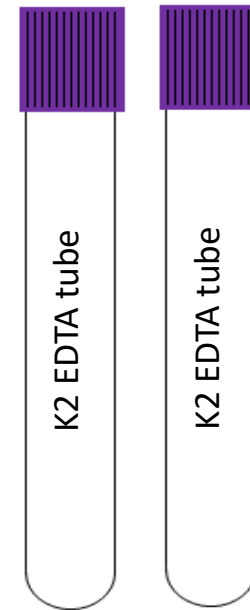
*Supplies provided for the collection of serum, plasma and buffy coat*



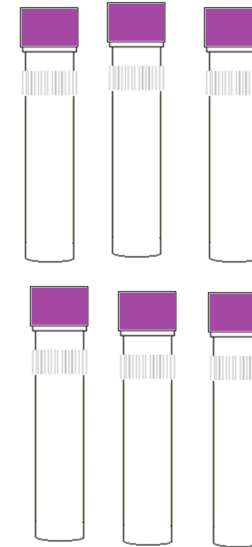
2 x 10ml Serum (plastic) collection tubes



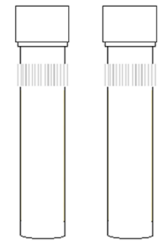
6 x 2ml Cryovials (red-capped) for plasma aliquots



2 x 10ml EDTA (purple-capped) for plasma aliquots

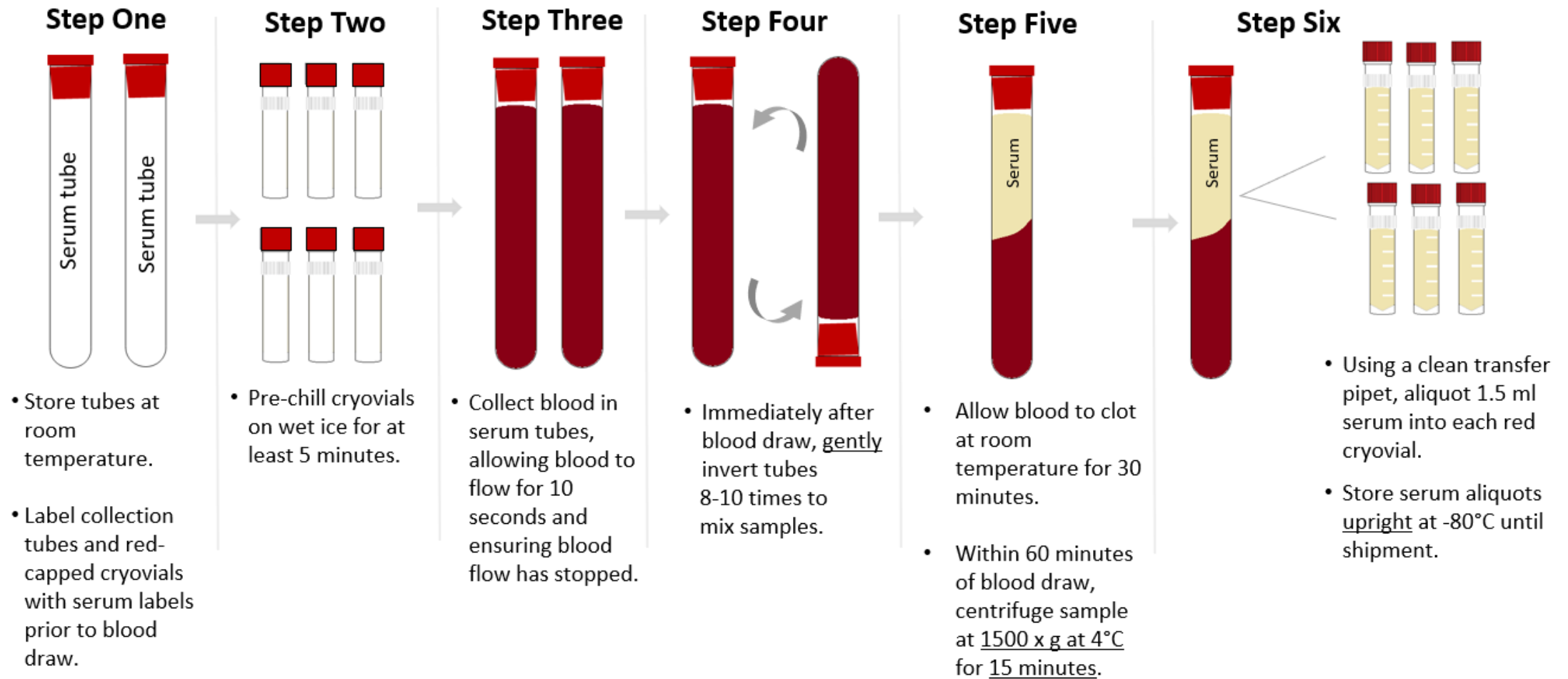


6 x 2ml Cryovials (purple-capped) for plasma aliquots

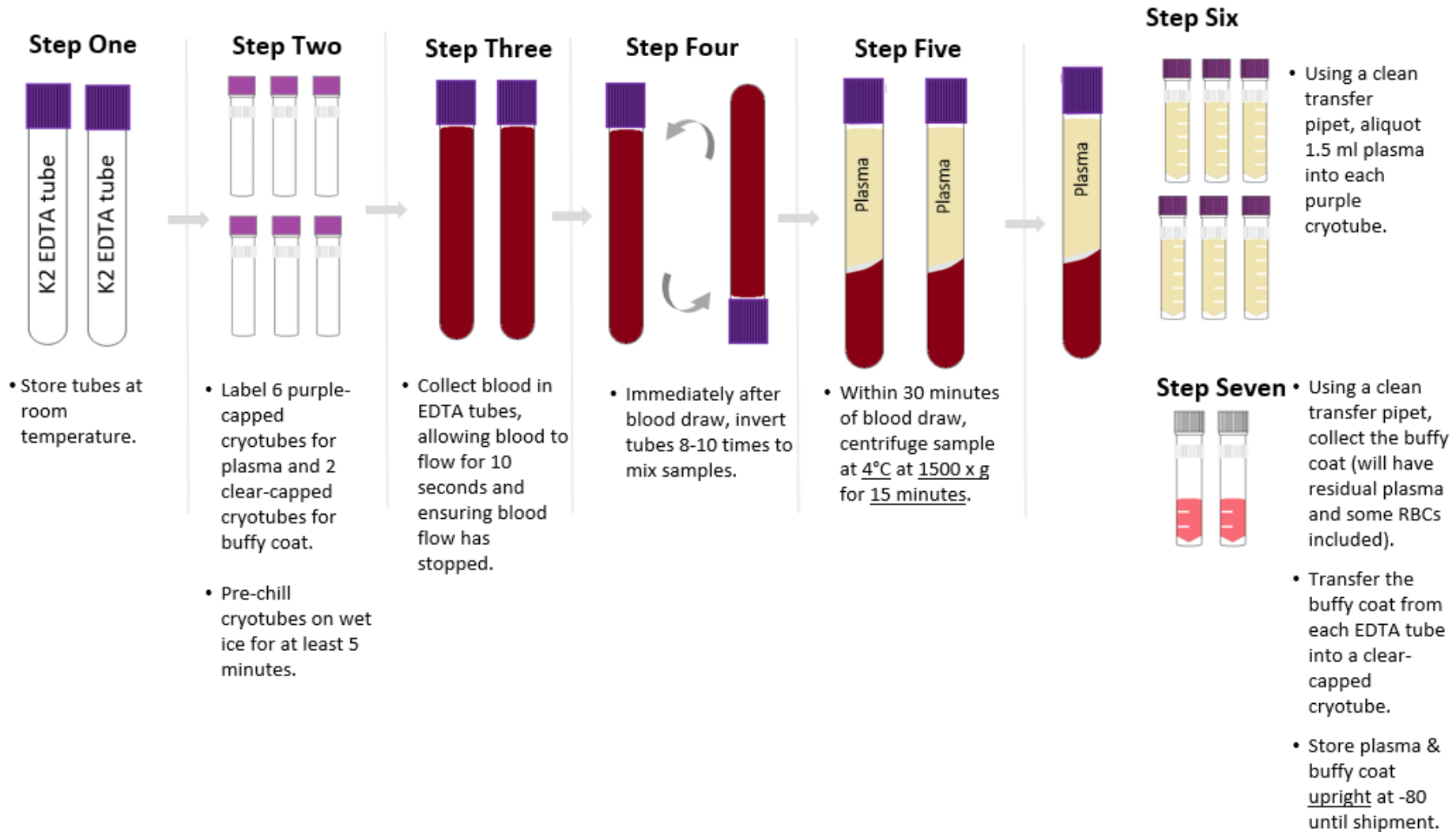


2 x 2ml Cryovials (clear-capped) for buffy coat aliquots

# Sample Collection and Processing: Serum



# Sample Collection and Processing: Plasma & Buffy Coat

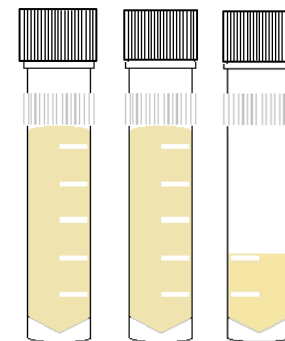


# Sample Collection and Processing: Aliquots

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Filling biomarker plasma and serum aliquots:

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



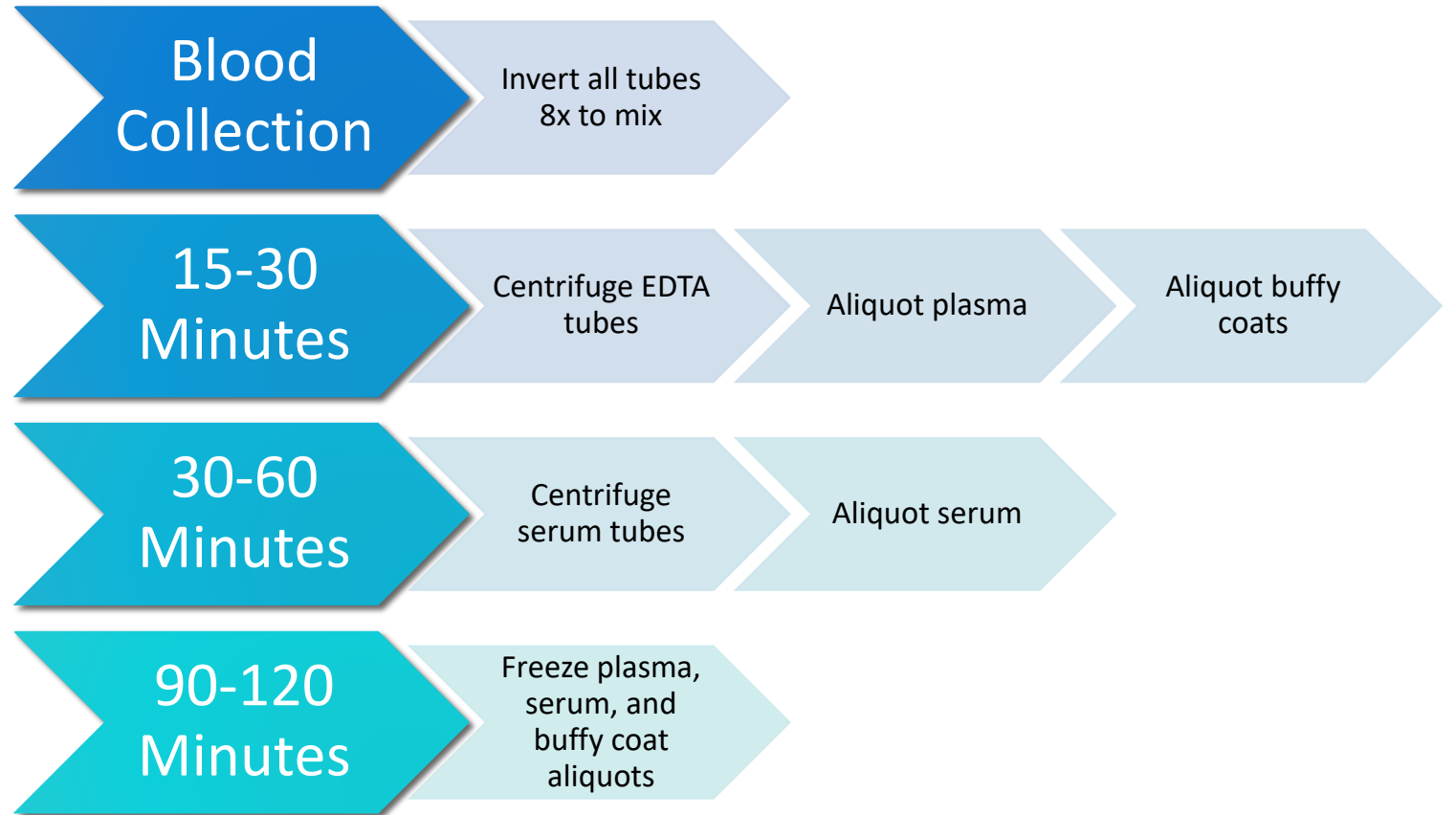
YES



NO

# Sample Collection and Processing: Timeline

Timeline for blood processing



# Sample Collection and Processing: Issue #1

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## 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

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## 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](http://www.bd.com/vacutainer/pdfs/techtalk/TechTalk_Jan2004_VS7167.pdf)



# Sample Collection and Processing: Issue #2 continued

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## 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](http://www.bd.com/vacutainer/pdfs/techtalk/TechTalk_Jan2004_VS7167.pdf)

# Sample Collection and Processing Form

Specimen Collection and Processing Form

Direct Link for Duke:

<https://redcap.link/DXCTEIISampleForm>

First page captures basic subject and visit information

**BioSEND** Returning?

Biospecimen Exchange for Neurological Disorders

Please complete the Specimen Collection and Processing Form, below.

Page 1 of 2

Diagnose Chronic Traumatic Encephalopathy Phase II (DxCTEII)

Study

Study Site

Email address of staff member completing this form

*Note: A copy of the completed sample form and the shipping manifest will be sent to this address.*

GUID:

Sex (used for DNA quality control)

Visit

IU Kit Number

# 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

1. SERUM (red-top tubes, 10 mL)

Was blood collected and processed for SERUM?

Yes

No

reset

Time of SERUM tube centrifugation   Now H:M  
Use 24 Hour clock

Duration of SERUM tube centrifugation   
minutes

Rate of SERUM tube centrifugation   
x g

Temperature of SERUM tube centrifugation   
degrees Celsius

Total volume of SERUM collected   
mL

# 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.

## DxCTEII Frozen Shipping Manifest

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 [sub\_id].

Please print a copy of that document and include it in the Kit #[kit\_num] shipping container.

Study \_\_\_\_\_

Study Site: \_\_\_\_\_

GUID: \_\_\_\_\_

Visit: \_\_\_\_\_

IU Kit Number: \_\_\_\_\_

Date of blood collection: \_\_\_\_\_

### SERUM

Number of SERUM aliquots shipped: \_\_\_\_\_

### 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

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## Packing and Shipping Frozen Samples

- All DxCTEII 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



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

# Shipping Samples

Packing and Shipping Frozen Samples

Shipper's Declaration not Required.

Dry Ice amount must be in kilograms.

Note: 2 lbs. = 1 kg.

Airwaybills / airmails must have the following:  
1. Dry Ice; 9; UN 1845  
2.  $\frac{\text{Number}}{\text{(Number pkgs)}} \times \frac{\text{wt}}{\text{(wt)}} \text{ Kg}$

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

The image shows a Class 9 Dry Ice Label template. It features a central diamond shape with a dashed border and a solid border. Inside the diamond, there are several vertical bars of varying heights. The label includes instructions for shipper's declaration, dry ice amount, and airwaybill requirements. It also has fields for shipper's name and address, consignee name and address, and a field for the net weight of dry ice in kilograms. The label is annotated with red arrows and text explaining the fields: '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 name and address field. The label also includes the text 'UN 1845' and '9'.

# 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 shipping interface for Indiana University School of Medicine. The header includes the IU logo and the text "INDIANA UNIVERSITY SCHOOL OF MEDICINE". Below the header, the text "and Affiliated Biorepositories" is displayed. The interface is divided into two main sections: "Ship From" and "Shipment Information".

**Ship From Section:**

- Search for address: A search bar with a magnifying glass icon and a "Clear" button.
- Code: Input field.
- Company: Icahn School of Medicine - Mt. Sinai
- Contact: Kenny Persaud
- Address 1: 1425 Madison (Icahn Building)
- Address 2: Icahn L4 39
- Address 3: Input field.
- City: New York
- State/Province: NY
- Postal Code: 10029
- Country/Territory: United States

**Shipment Information Section:**

- Study Group: SSBC (dropdown menu)
- Weight: 20 (input field) LB (dropdown menu)
- Dry Ice Weight: 10 (input field) LB (dropdown menu)
- Description of Return: Biologic Specimens
- Pickup Request: Button

**Annotations:**

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

**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



BILLING: P/P  
DESC: Biological Specimens  
RETURN SERVICE

Reference No. 1: 4087277

XOL 20.03.09 NV45 83.0A 12/2019



# Shipping Samples: Closures

Date	Holiday
January 1	New Year's Day
3 <sup>rd</sup> Monday in January	Martin Luther King, Jr Day
4 <sup>th</sup> Monday in May	Memorial Day
June 19	Juneteenth (observed)
July 4	Independence Day (observed)
1 <sup>st</sup> Monday in September	Labor Day
4 <sup>th</sup> Thursday in November	Thanksgiving
4 <sup>th</sup> 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

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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

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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

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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***

# Contacts

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## Indiana University

General Questions/Shipment Notifications:

[biosend@iu.edu](mailto:biosend@iu.edu)

317-278-6158

Request kits:

<https://redcap.link/dxctellkits>