



Chronic Subdural Hematoma Treatment with Embolization Versus Surgery Study (BioCHESS)

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 - Blood

Collection Tube	Drawn At	Specimen Type	Aliquot Volume	Total Number of Aliquots	Cryovial Cap Color	Shipping Temperature
1 EDTA (plastic) Blood Collection Tubes, 10ml	Baseline	Plasma	1.5ml	3	Purple	Frozen
	Baseline	Buffy Coat	~750ul	1	Clear	Frozen
1 SERUM (plastic) Blood Collection Tubes, 10ml	Baseline	Serum	1.5ml	3	Red	Frozen

Biospecimen Collection Protocol - Tissue

Collection Tube	Drawn At	Specimen Type	Aliquot Volume	Total Number of Aliquots	Shipping Temperature
2 Prefilled Formalin Tubes, Green-top, 30ml 2	Baseline	Membrane	1 section	1	Ambient
	Baseline	Dura	1 section	1	Ambient
2 Prefilled <i>RNA Later</i> TM Tubes, Green-top, 30ml	Baseline	Membrane	1 section	1	Ambient
	Baseline	Dura	1 section	1	Ambient
2 Green-top Tubes Fresh Frozen (no preservative), 30ml	Baseline	Membrane	1 section	1	Frozen
	Baseline	Dura	1 section	1	Frozen
Individually wrapped conical tube, 15ml	Baseline	Subdural Hematoma Fluid	15ml	1	Frozen

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
 - Includes barcoded labels, collection, processing, and shipping supplies specific to each visit
 - The contents of a kit are not tied to a specific subject or time point but each kit should only be used for 1 subject

Kit Contents and Ordering – REDCap Survey

<https://redcap.link/biochesskitrequest>

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 logo for BioSEND features the word "Bio" in a dark blue, sans-serif font, followed by "SEND" in a larger, bold, blue font. The letter "S" is stylized with a blue arrow that curves from the top of the "S" down to the bottom, and another blue arrow that curves from the bottom of the "S" up to the top.

Biospecimen Exchange for Neurological Disorders

NINDS Biosend BioCHESS Kit Request System

Study Site

* must provide value

Submit

AAA



Kit Contents and Ordering: Confirm Site Info

DxCTEII 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

BioCHESS 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 up to 2 subject's visits

Kit Type

****Please allow two weeks for shipment****

* must provide value

Blood and Tissue Collection Kit

Frozen Shipping Kit

Ambient Shipping Kit

Extra Supplies

Please specify in comments if you need kits before the standard two week shipment time.

Kit Contents and Ordering: Kit Breakdown

BioCHESS Kit Request Module

Comments

Expand

Each Blood Collection Kit contains:

- 1 - EDTA tube, 10ml (plastic)
- 1 - Serum tube, 10ml (plastic)
- 3 - Cryovial (Sarstedt®) with purple cap, 2ml
- 3 - Cryovial (Sarstedt®) with red cap, 2ml
- 1 - Cryovial (Sarstedt®) with clear cap, 2ml
- 1 - Individually wrapped conical, 15ml
- 2 - Prefilled Formalin tube, 30ml
- 2 - Prefilled *RNA Later*TM tube, 30ml
- 2 - Green top tube, 30ml
- 2 - Disposable pipette, 3ml
- 2 - Resealable tube pouch
- 1 - Cryobox, 25 slot
- 1 - Specimen/Case label set-- Kit numbers



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

Submit

Kit Contents and Ordering: Blood Kits



Kit Contents and Ordering: Shipping kits



Frozen shipping kit



Ambient shipping kit

Collection Volumes

Total blood volumes

Sample Type	Amount
Whole Blood for Plasma and Buffy Coat	10 ml
Whole Blood for Serum	10 ml

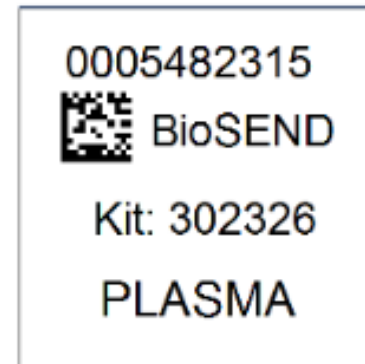
Kit and Supply Ordering

- 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

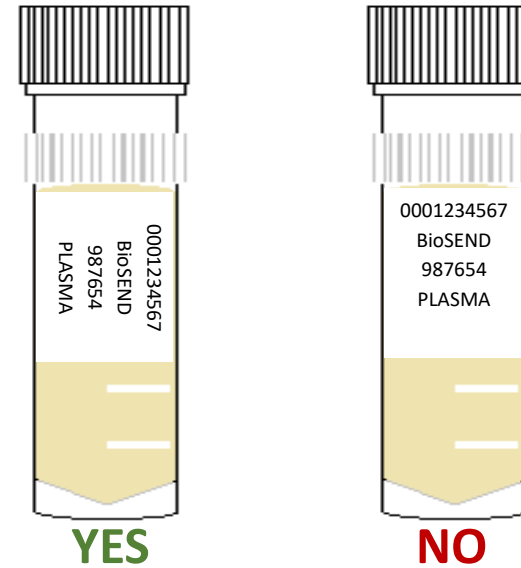
- Please check that all samples are properly labelled to ensure correct identification by IU
- If do not have enough labels to complete a visit, please contact IU *immediately*
- Labelling the tubes during processing prevents sample mix-ups



Sample Labelling: Label Placement

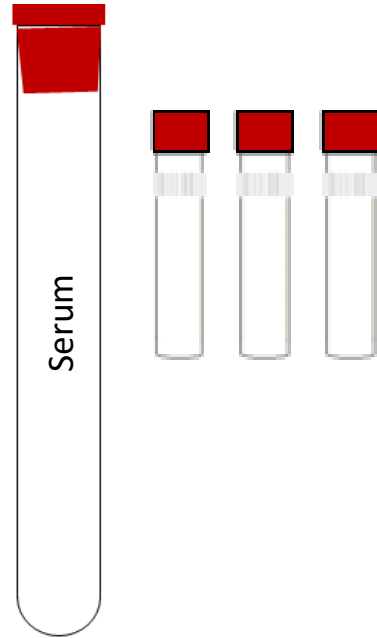
Please...

- 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 - Blood

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

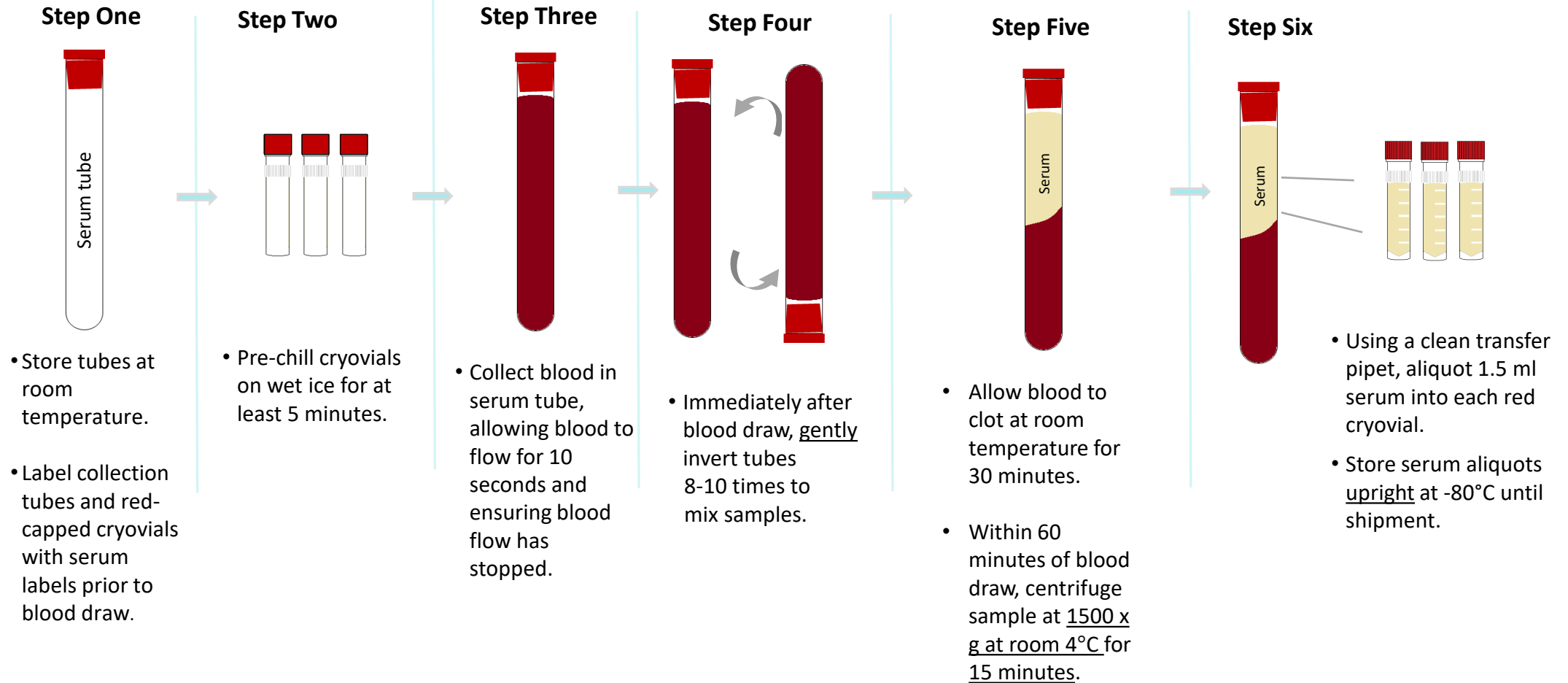


1 x 10ml Serum
(plastic) collection
tubes

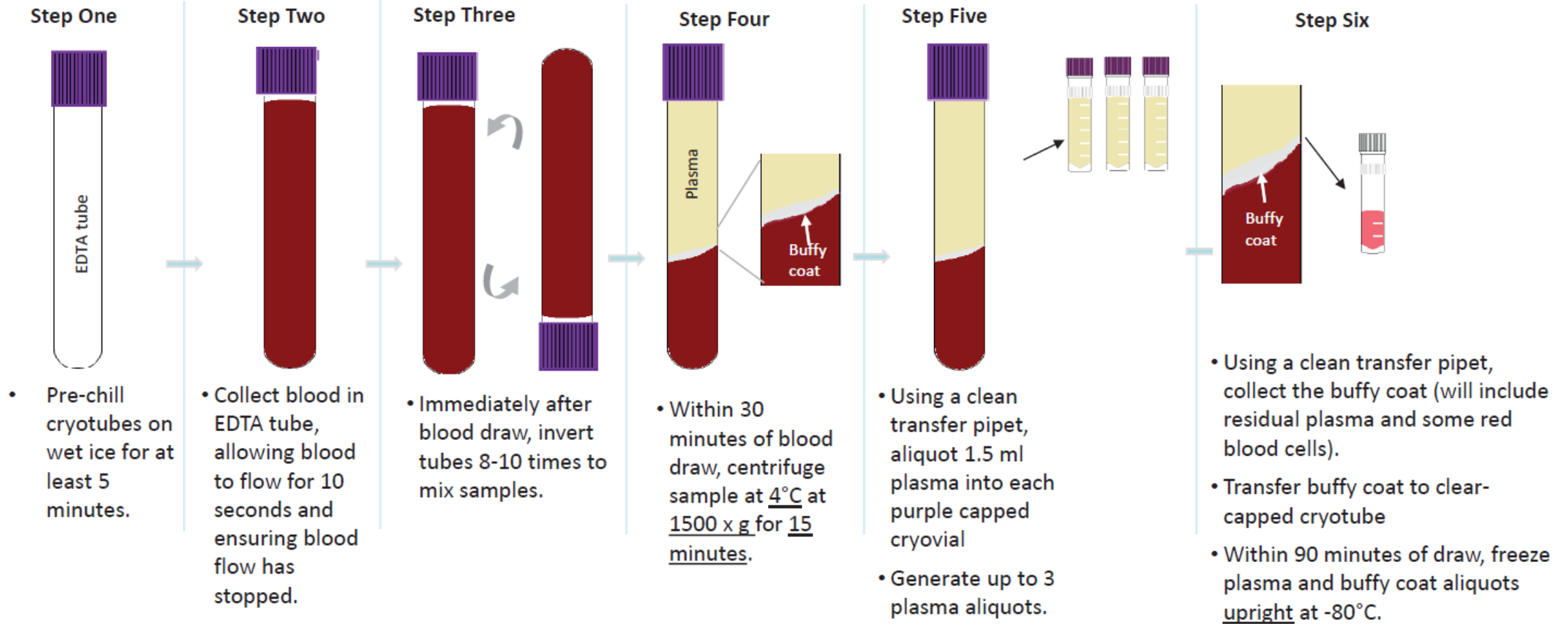


1 x 10ml EDTA
(plastic) collection
tubes

Sample Collection and Processing: Serum



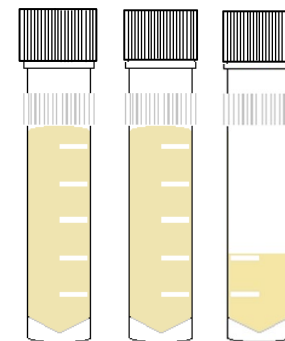
Sample Collection and Processing: Plasma & Buffy Coat



Sample Collection and Processing: Aliquots

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



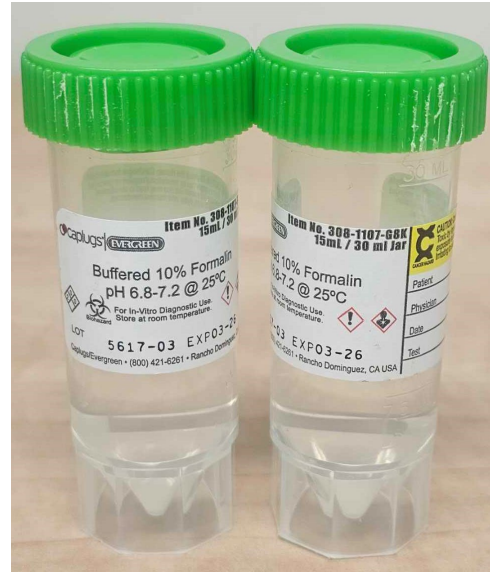
YES



NO

Sample Collection and Processing

Supplies provided for the collection of SDH Fluid, dura and membrane tissue in Formalin, RNALater, and Fresh Frozen (no preservative)



2 x 30ml tubes with pre-filled Formalin



2 x 30ml tubes with RNALater™



2 x 30ml tubes Fresh-frozen samples (no preservative)



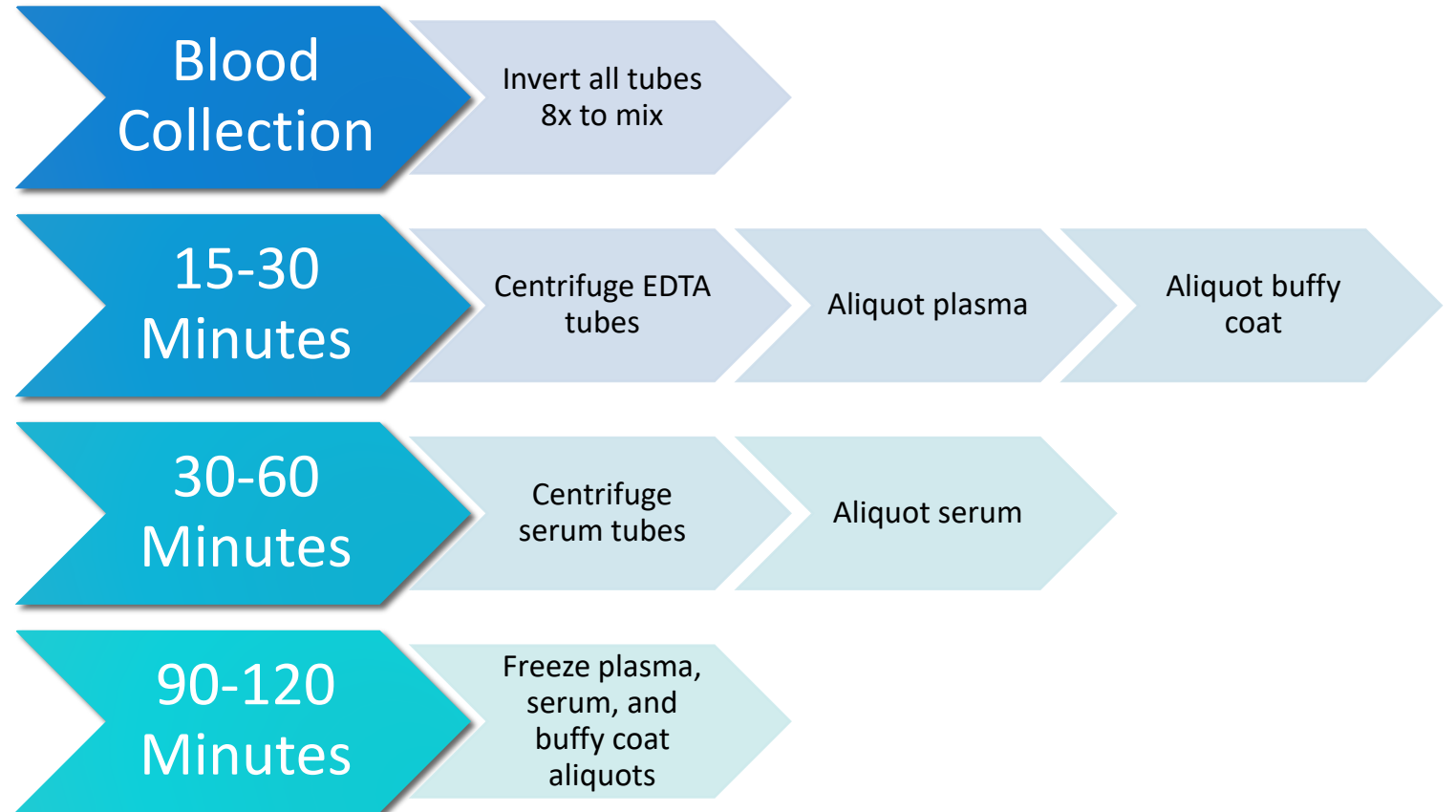
1 x 15ml tube for SDH Fluid

Sample Collection and Processing: Dura, Membrane, and SDH Fluid

- Please maintain the sterile field and avoid puncturing the brain
- Dissect and cut Dura and Membrane sample into three sections.
- Collect 15ml of SDH Fluid and place in sterile conical
- Tissue samples for Dura and Membrane will be collected in the following order priority (1) Formalin, (2) *RNALater*[™], and (3) fresh frozen (no preservative).
- Fully submerge Dura and Membrane tissue in Formalin and *RNALater*[™]
- Tighten caps on all tubes to avoid leaking in transit

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

Specimen Collection and Processing Form

Direct Link for Duke:

<https://redcap.link/BioCHESSSampleForm>

First page captures basic subject and visit information

BioSEND

Biospecimen Exchange for Neurological Disorders

Protocol: BioCHESS

Please complete the Specimen Collection and Processing Form, below.

Returning?

AAA



Page 1 of 4

Study Site

Email address of staff member completing this form

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

BioCHESS Subject ID:

Subject's biological sex (used for DNA quality control)

IU Kit Number

7 characters remaining

Next Page >>

Save & Return Later

Sample Collection and Processing Form


Second page captures processing information


BioSEND

Biospecimen Exchange for Neurological Disorders

Page 2 of 4

Tissue Collection

Date of tissue collection  Today M-D-Y

Time of tissue collection  Now H:M
Use 24 Hour clock.

Was Dura collected in Pre-filled formalin?

[reset](#)

Was Dura collected in Pre-filled RNALater?

[reset](#)

Was Dura collected for Fresh Frozen (no preservative)?

[reset](#)

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.

Confidential

Page 1

BioCHESS 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 [subj_id].

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

Study Site:

BioCHESS Subject ID:

IU Kit Number:

Tissue

Date of tissue collection:

Dura shipped fresh frozen (no preservative)

Membrane shipped fresh frozen (no preservative)

SDH Fluid

Volume of SDH fluid shipped

Serum

Date of blood collection:

Number of SERUM aliquots shipped:

PLASMA EDTA

Number of PLASMA EDTA aliquots shipped:

Number of BUFFY COAT aliquots shipped:

Sample Collection and Processing Form

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

BioCHESS Ambient Shipping Manifest

Please verify/update the information below. When you click the "Submit" button below, a PDF copy of the Ambient 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 with Kit #[kit_num].

Because no samples were fixed in formalin, all specimens should be shipped frozen. Click SUBMIT to skip this form.

Please verify that the caps on the formalin tubes are screwed on tightly to prevent leakage in transit.

Study Site:

BioCHESS Subject ID:

IU Kit Number:

Dura shipping in formalin

Membrane shipping in formalin

Dura shipped in RNALater

Membrane shipped in RNALater

Date of collection:

Time of collection:

(24-hour clock)

Shipping Information - Please complete.

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 Frozen and Ambient 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

- Serum, Plasma, Buffy coat, Subdural Hematoma Fluid, and fresh frozen (no preservative) Dura / Membrane sections will ship frozen on dry ice
- Please verify that the cap on the SDH Fluid tube is screwed on tightly to prevent leakage in transit.
- 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 Ambient Samples: Tips

Packing and Shipping Ambient Samples

- Dura / Membrane sections in Formalin and *RNALater*TM will ship Ambient
- Ambient samples should be shipped same day as collection
- Please verify that the caps on the formalin tubes are screwed on tightly to prevent leakage in transit



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 / airbills 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 seven vertical bars of varying heights. The label includes instructions for completion, such as 'Shipper's Declaration not Required' and 'Dry Ice amount must be in kilograms'. It also provides a formula for calculating the weight of dry ice in kilograms based on the number of packages and the weight of each package. The label is divided into sections for 'Shipper's Name and Address' and 'Consignee Name and Address'. The text 'UN 1845' is prominently displayed in the center. Red arrows point to specific fields with explanatory text: 'Net weight of dry ice in kg' points to the 'kg.' 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 number '9' is located at the bottom center of the diamond, and the code '06426 1/01 RRD' is at the bottom left.

Shipping Samples: Frozen

Do not ship more than 2 biohazard bags in a single shipper (equivalent to 2 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 the Indiana University School of Medicine. The header features 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 LB (input field and dropdown menu)
- Dry Ice Weight: 10 LB (input field and dropdown menu)
- Description of Return: Biologic Specimens
- Pickup Request: A blue button.

Annotations:

- "Search for address": A dashed box around the search bar with a blue arrow pointing to it.
- "Choose Study": A dashed box around the "Study Group" dropdown with a blue arrow pointing to it.
- "Enter weight": A dashed box around the "Weight" and "Dry Ice Weight" fields with a blue arrow pointing to them.
- "Schedule Pickup": A dashed box around the "Pickup Request" button with a blue arrow pointing to it.
- "Click 'Ship'": A dashed box around the "Ship" button at the bottom right with a blue arrow pointing to it.

Buttons:

- Clear (blue button)
- Pickup Request (blue button)
- Reset (blue button)
- Ship (blue button)

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 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***

Contacts

Indiana University

General Questions/Shipment Notifications:

biosend@iu.edu

317-278-6158

Request kits:

<https://redcap.link/biochesskitrequest>

Request sample form:

<https://redcap.link/BioCHESSSampleForm>