



Brain Structure and Clinical Endpoints in Myotonic Dystrophy Type 2 (BraCE-DM2)

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 | Cryovial Cap Color | Shipping Temperature |
|---|----------|---------------|----------------|--------------------------|--------------------|----------------------|
| 2 EDTA (glass) Blood Collection Tubes, 10ml | Visit 1 | Plasma | 1.5ml | 6 | Purple | Frozen |
| | Visit 1 | Buffy Coat | ~750ul | 2 | Clear | 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
 - 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

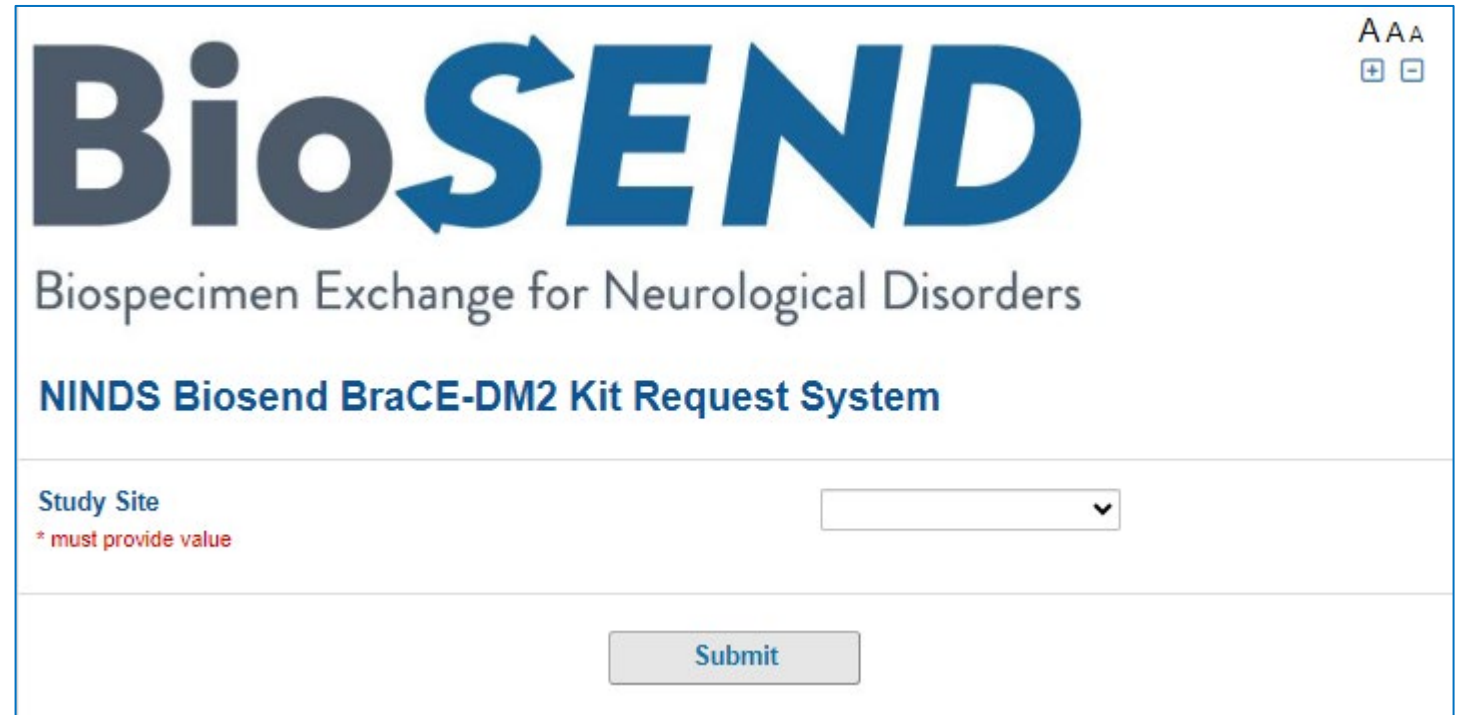
Kit Contents and Ordering – REDCap Survey

<http://kits.iu.edu/biosend/bracedm2>

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 'NINDS Biosend BraCE-DM2 Kit Request System' interface. At the top is the 'BioSEND' logo, where 'Bio' is in a dark blue sans-serif font and 'SEND' is in a larger, bold blue sans-serif font with a curved arrow around the 'S'. Below the logo is the text 'Biospecimen Exchange for Neurological Disorders'. The title 'NINDS Biosend BraCE-DM2 Kit Request System' is displayed in a bold blue font. A form field labeled 'Study Site' is present, with a red asterisk and the text '* must provide value' below it. To the right of the label is a dropdown menu. In the top right corner, there are three small icons: 'A A A' and two square buttons with '+' and '-' signs. A 'Submit' button is located at the bottom right of the form area.

BioSEND
Biospecimen Exchange for Neurological Disorders
NINDS Biosend BraCE-DM2 Kit Request System

Study Site ▼
* must provide value

Submit

Kit Contents and Ordering: Confirm Site Info

BraCE-DM2 Kit Request Module

| | | |
|---|--|--|
| Study Site <small>* must provide value</small> | Indiana Univers | 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

BraCE-DM2 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** <small>* must provide value</small> | <div><input checked="" type="checkbox"/> Blood Collection Kit</div> <div><input type="checkbox"/> Shipping Kit</div> <div><input type="checkbox"/> Extra Supplies</div> <p>Please specify in comments if you need kits before the standard two week shipment time.</p> |
| Blood Collection Kit Quantity <small>* must provide value</small> | <input type="text" value="3"/> |
| Comments | <div><input type="text"/></div> <div>Expand</div> |

Kit Contents and Ordering: Kit Breakdown

BraCE-DM2 Kit Request Module

Comments

Expand

Each Blood Collection Kit contains:

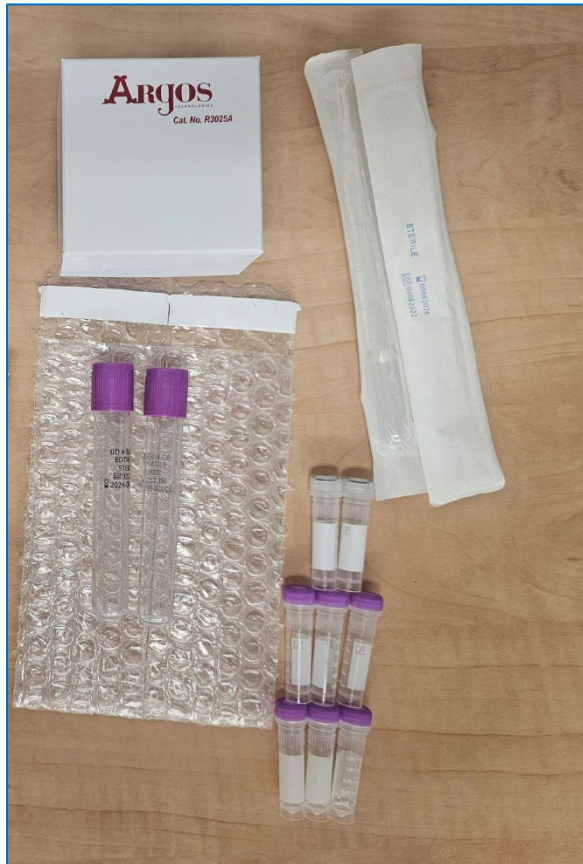
- 2 - EDTA tube, 10ml (glass)
- 6 - Cryovial (Sarstedt®) with purple cap, 2ml
- 2 - Cryovial (Sarstedt®) with clear cap, 2ml
- 2 - Disposable pipette, 3ml
- 2 - Resealable tube pouch
- 1 - Cryobox, 25 slot
- 1 - Specimen/Case label set (kit numbers)

Submit

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

Kit Contents and Ordering: Kits

Blood Kit (frozen):



Shipping Kit:



Collection Volumes

Total blood volumes

| Sample Type | Amount |
|---------------------------------------|--------|
| Whole Blood for Plasma and Buffy Coat | 20 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

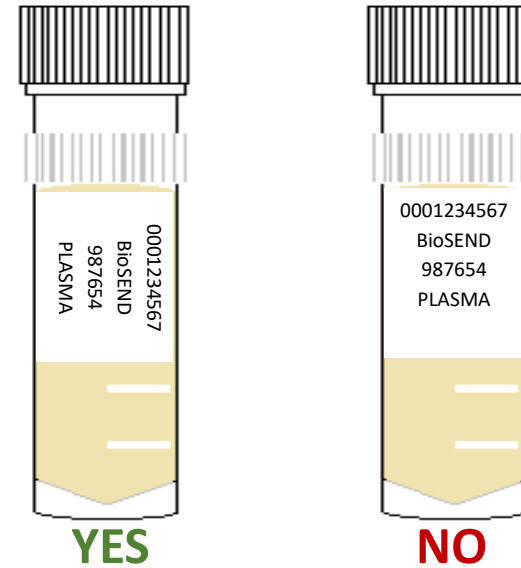
- Please check that all samples are properly labelled to ensure correct identification by IU
- If do not have enough labels to complete a visit, please contact IU *immediately*
- Labelling the tubes during processing prevents sample mix-ups



Sample Labelling: Label Placement

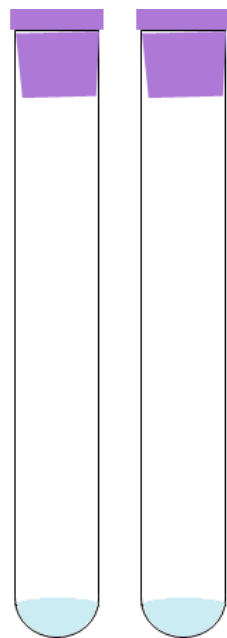
Please...

- 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

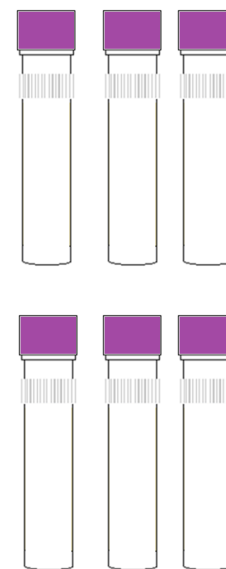


Sample Collection and Processing

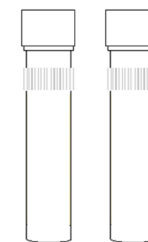
*Supplies provided for the collection of
plasma and buffy coat*



2 x 10ml EDTA (glass)
collection tubes

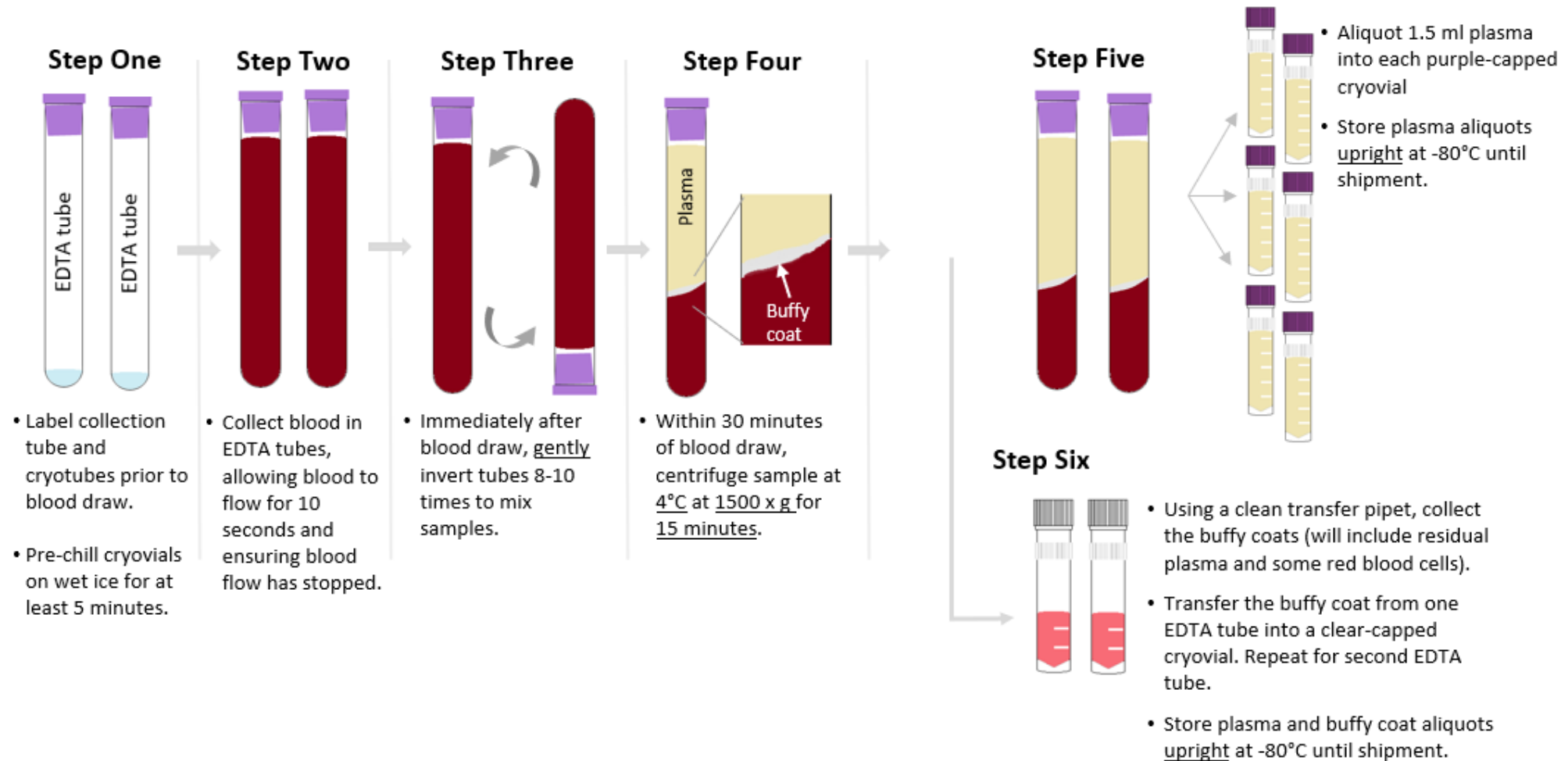


6 x 2ml Cryovials
(purple-capped) for
plasma aliquots



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

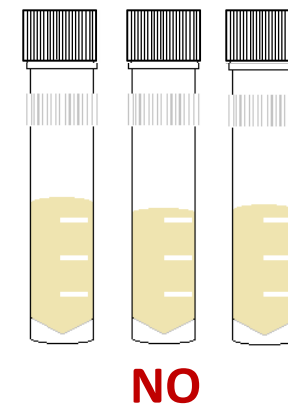
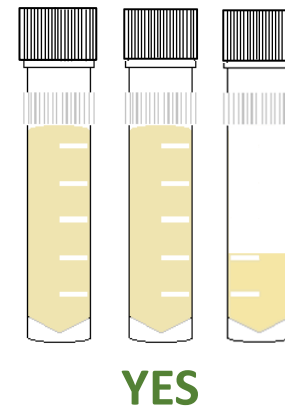
Sample Collection and Processing: Plasma & Buffy Coat



Sample Collection and Processing: Aliquots

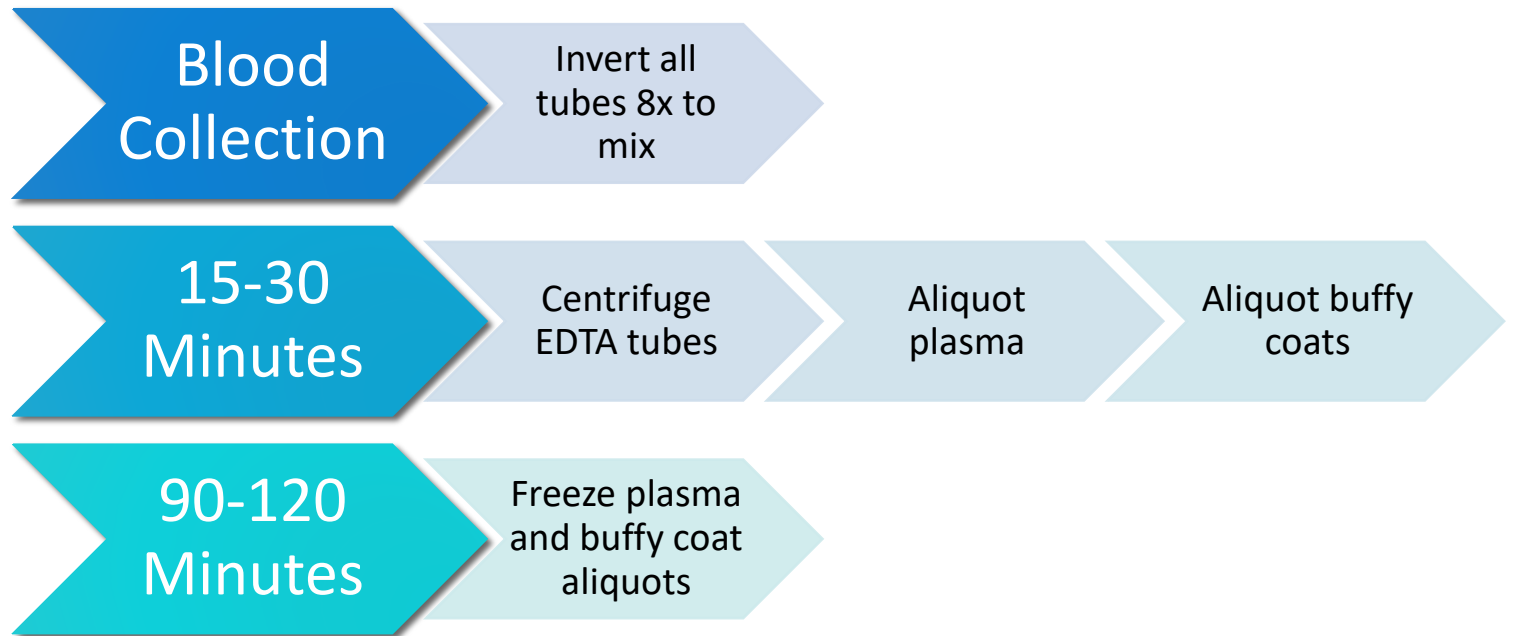
Filling biomarker plasma aliquots:

- 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



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:

<https://redcap.link/BRACEDM2SampleForm>

First page captures basic subject and visit information



Biospecimen Exchange for Neurological Disorders

Please complete the Specimen Collection and Processing Form, below.

[Returning?](#)

A A A



Page 1 of 2

BioSEND BraCE-DM2 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

6 characters remaining

[Next Page >>](#)

[Save & Return Later](#)

Sample Collection and Processing Form

Direct link:

<https://redcap.link/BRACEDM2SampleForm>

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

Temperature of PLASMA EDTA tube centrifugation

degrees Celsius

Sample Collection and Processing Form

Direct link:

<https://redcap.link/BRACEDM2SampleForm>

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

BraCE-DM2 Frozen Shipping Manifest

Page 1

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: ☐ Wake Forest

GUID:

Visit: ☐ V1

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 samples ship frozen 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!

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


Shipping Samples: Frozen

Shipping kits contain the supplies to ship two cryoboxes

- 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>

**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

Ship From

Clear

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

Pickup Request

SSBC

20

LB

10

LB

Biologic Specimens

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 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:

<http://kits.iu.edu/biosend/bracedm2>