



Biospecimen Exchange for Neurological Disorders

Intermediate-Size Expanded Access Trial of Autologous Hybrid  
TREG/Th2 Cell Therapy (RAPA-501) of Amyotrophic Lateral Sclerosis

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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 1500 RCF (x g)
- -80°C Freezer
- Dry ice

# Procedures

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MAINTAINING SPECIMEN UNIFORMITY AND QUALITY

# Biospecimen Collection Protocol

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Sample Type & Volume	Screening/BL Day 0	Apheresis	Cycle 1 Day 1 (D35) ± 14	Cycle 2 Day 1 (D77) ± 14	Cycle 3 Day 1 (D119) ± 14	Cycle 4 Day 1 (D161) ± 14	Follow-up Visit (D190) ± 14
Serum aliquots, 1.5ml	3	3	3	3	3	3	3

# 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/rapakit>  
s

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.

**BioSEND**  
Biospecimen Exchange for Neurological Disorders

Protocol: RAPA-501-ALS-EAP (Intermediate-Size Expanded Access Trial of Autologous Hybrid TREG/Th2 Cell Therapy (RAPA-501) of Amyotrophic Lateral Sclerosis)

Please order kits and supplies below. Email [biosend@iu.edu](mailto:biosend@iu.edu) with any questions.

**Study Site**  
\* must provide value

Submit

# Kit Contents and Ordering: Confirm Site Info

RAPA-501-EAP Kit Request Module

<b>Study Site</b> <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		
<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

## RAPA-501-EAP 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.
- Shipping Kits are ordered independently of Blood Kits
- A single Shipping Kit may be used to send samples for up to 18 visits

<b>Kit Type</b> **Please allow two weeks for shipment** * must provide value	<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>
<b>Blood Collection Kit Quantity</b> * must provide value	<input type="text"/>
<b>Comments</b>	<div><input type="text"/></div> <div>Expand</div>

# Kit Contents and Ordering: Kit Breakdown

RAPA-501-EAP Kit Request Module

<b>Comments</b>	
	<div></div> <div>Expand</div>
<b>Blood Collection Kit</b>	
<b>Blood Collection Kit Contents:</b> 1 - Red-top Serum tube (10ml) plastic 3 - Red-capped cryovial (Sarstedt), 2ml 1 - Disposable transfer pipette (3ml) 10 - Cryohold specimen labels-- Kit numbers	

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

# Kit Contents and Ordering: Blood & Shipping Kits

Blood Kit (frozen):



Shipping Kit:



# 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

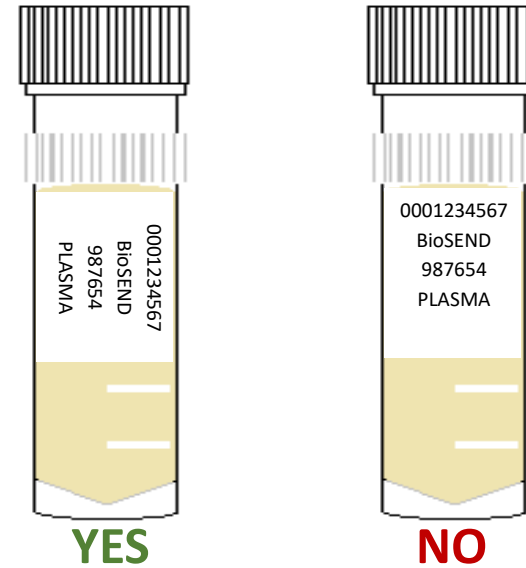


# Sample Labelling: Label Placement

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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



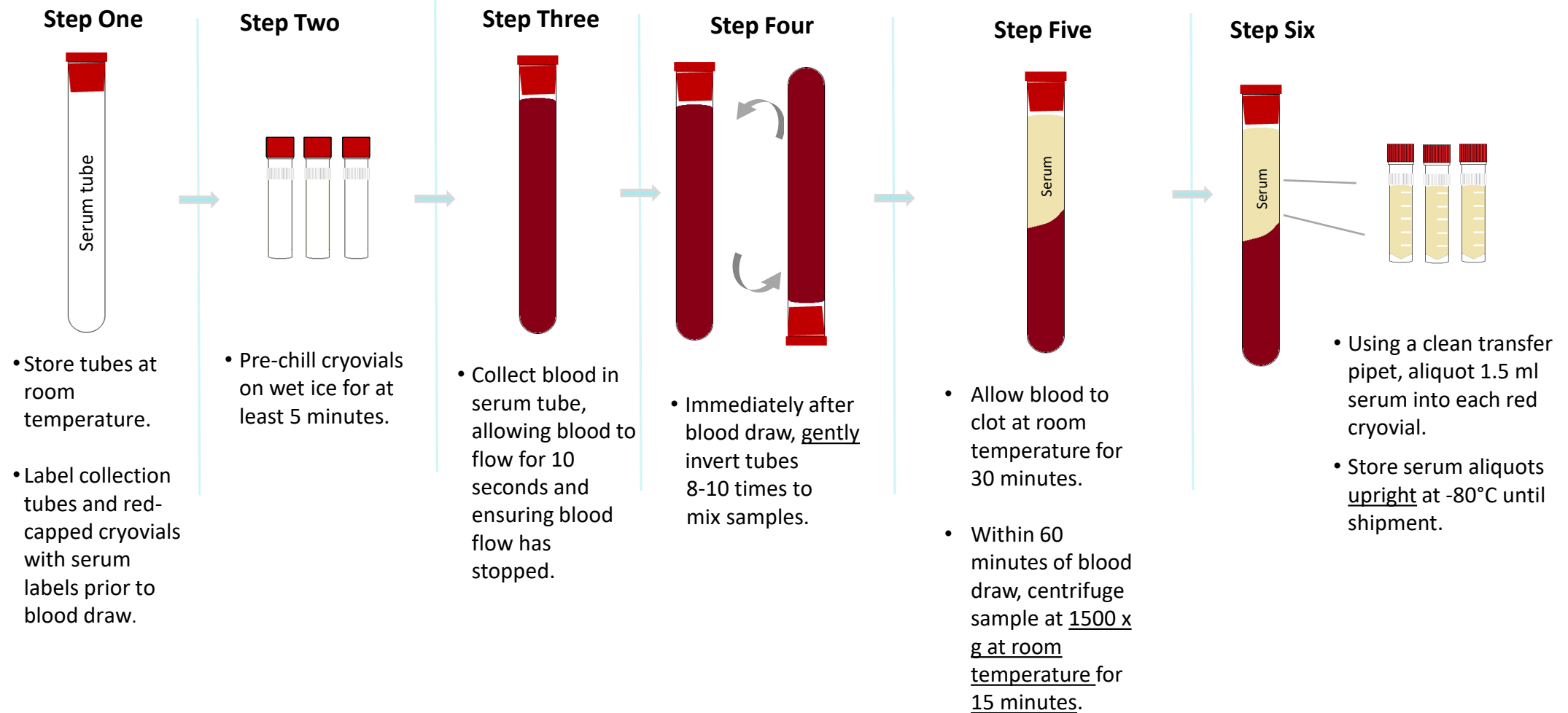
# Sample Collection and Processing

*One 10ml plastic serum tube is  
provided for the collection and  
processing of serum*

1 x 10ml Serum  
tubes



# Sample Collection and Processing: Serum

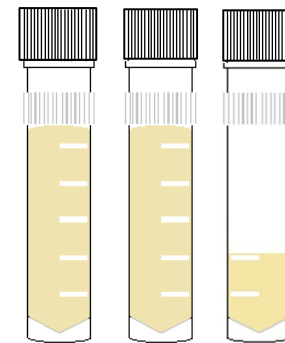


# Sample Collection and Processing: Aliquots

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Filling biomarker serum aliquots:

- Fill as many cryovials as possible to 1.5 ml
- 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: 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 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 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:

<https://redcap.link/RAPASampleForm>

First page captures basic subject and visit information



Returning?

AAA



Biospecimen Exchange for Neurological Disorders

Protocol: RAPA-501-ALS-EAP (Intermediate-Size Expanded Access Trial of Autologous Hybrid TREG/Th2 Cell Therapy (RAPA-501) of Amyotrophic Lateral Sclerosis)

Please complete the Specimen Collection and Processing Form, below. Email [biosend@iu.edu](mailto:biosend@iu.edu) with any questions.

Page 1 of 2

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.*

RAPA-501-ALS-EAP Subject ID:   
ex. 501-EAP-01-003

Subject's sex (used for DNA quality control)

Visit

Kit Number   
7 characters remaining  
6-7 digit number on BioSEND labels

Next Page >>

Save & Return Later

# Sample Collection and Processing Form

Second page captures processing information

AAA

+

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BioSEND

Biospecimen Exchange for Neurological Disorders

Page 2 of 2

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

Use 24 hour clock

SERUM (One 10ml Red-top Tube)

Was blood collected for SERUM?

Yes

No

reset

Blood volume collected for SERUM

mL

Time of SERUM tube centrifugation

Now

H:M

Use 24 hour clock

Duration of SERUM tube centrifugation

15

minutes

Rate of SERUM tube centrifugation

1500

x g

Was SERUM tube centrifuged at room temperature?

Yes

No

reset

# Sample Collection and Processing Form

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

Confidential

Page 1

## RAPA ALS 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: ☐ Mass General Hospital

RAPA ALS Subject ID:

Visit: ☐ BL  
☐ D35  
☐ D77  
☐ D119  
☐ D161  
☐ D190

IU Kit Number:

Date of blood collection:

### SERUM

Number of SERUM aliquots shipped:

### WHOLE BLOOD

Number of Whole Blood tubes 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 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?

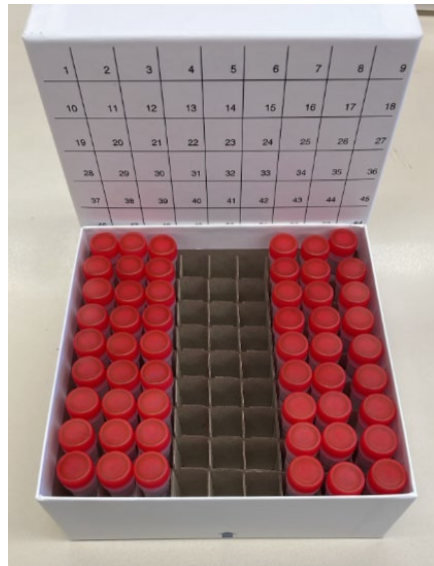
# Sample Collection and Processing Form

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 Samples: Frozen

Serum aliquots will be stored in an 81-slot cryobox as they are collected. Once a cryobox is filled completely (i.e., contains 18 visits), the cryobox should be shipped to BioSEND. Specimens should be shipped on at least a quarterly basis (i.e., every 3 months). If a cryobox is not filled completely at the end of the quarter, the partial cryobox should still be shipped to BioSEND.



# Shipping Frozen Samples: Tips

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## Packing and Shipping Frozen Samples

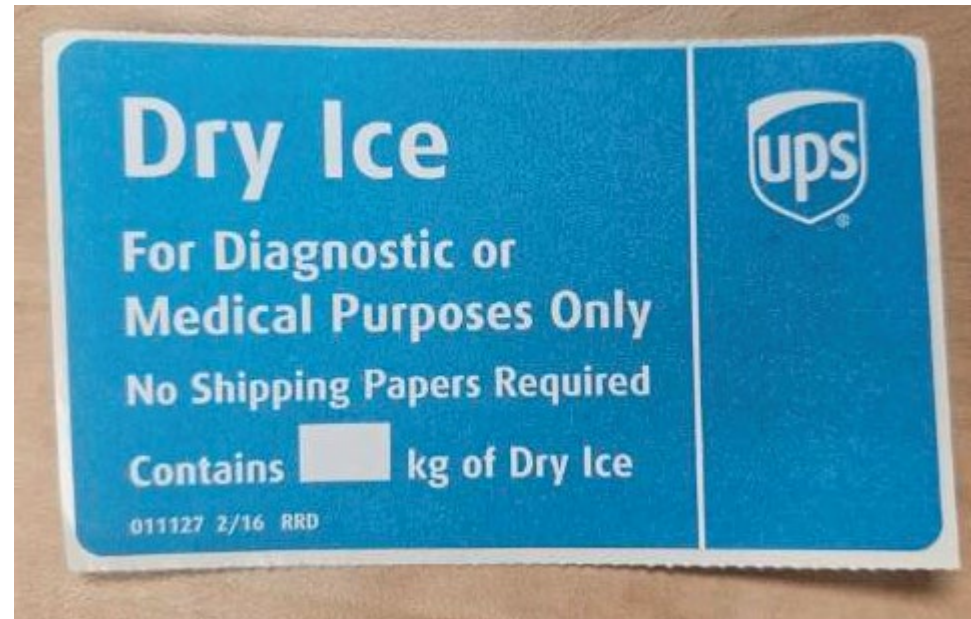
- Serum ship frozen on dry ice
- Frozen samples should be shipped **only** Monday through Wednesday
- Always fill carton to **top** with dry ice
- Do not pack shipment until the day of pickup



# Shipping Samples

Packing and Shipping Frozen  
Samples

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



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

**INDIANA UNIVERSITY**  
SCHOOL OF MEDICINE

and Affiliated Biorepositories

**Ship From**

Search for address

Code

Company

Contact

Address 1

Address 2

Address 3

City

State/Province

Postal Code

Country/Territory

**Shipment Information**

Study Group

Weight

Dry Ice Weight

Description of Return

Pickup Request

Choose Study

Enter weight

Click "Ship"

Schedule Pickup

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 <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 serum within 2 hours of collection allows for breakdown of certain proteins and small molecules
- Over/under centrifuging changes specimen 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***

# 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](mailto: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](mailto: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

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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/rapakits>