

HEAD-to-head Evaluation of tau tracers in Alzheimer's Disease

in collaboration with

**The National Centralized Repository for Alzheimer's Disease and Related
Dementias (NCRAD)**

Blood-Based Biospecimen Training Slides

Contact Information

- Questions?

Please contact NCRAD Coordinators at:

- Phone: 317-274-7890
- CRC email: dlkeys@iupui.edu
- Back-up email: alzstudy@iu.edu
- Website: www.ncrad.org



NCRAD

Training Overview:

- Blood-Based Collection Schedule
- Kit Request Module
- Specimen Labels
- Handling/Processing Study Specimens
- Sample Shipping
- NCRAD Website
- Questions?

HEAD Biospecimen Collection Schedule

Specimen Type	Baseline Visit	18 Month Visit
**Whole Blood for RNA	X	X
Serum	X	X
Plasma	X	X
DNA	X	X
Whole Blood for Banking	X	X

****2.5 ml PAXgene™ Blood RNA Tube**

Kit Request Module

<https://kits.iu.edu/head>



Kit Request Module

- An initial stock of kits will be delivered prior to the designated site specific start date.
- Kits and individual supplies are available to order:
 - Blood-Based Kit
 - Frozen Blood Shipping Supply Kit
 - Blood-Based Supplemental Supply Kit (1 only at study start up)
 - Individual Supplies

NCRAD Kit Request Module



NCRAD

1. Choose your site from the drop down list
2. The coordinator name and contact information will appear
3. Verify that this information is accurate, correct if necessary

Study Site * must provide value

007- Mayo Clinic

Attn: Julie Simonson

Address: Mayo Clinic
Charlton 6, 200 First ST SW
Rochester MN 55905

Phone: 507-422-5406

Email: Block.Britten@mayo.edu

Reminder: Please allow two weeks for kit orders to be processed and shipped

Is the contact name above correct? Yes No * must provide value [reset](#)

Contact New Name * must provide value

Kits Available

HEAD Blood Collection Kits

Total Number of Blood Collection Kits Requested
(same collection for BL, month 18)

Total Number of Blood Supplemental Kits Requested
Typically one per site per year

Total Number of Frozen Blood Shipping Kits Requested
Includes small frozen shipper

HEAD Frozen Shipping Kits

Total Number of Frozen Shipping Kits Requested
*For batch shipments of 5-6 cryoboxes

Study Visit Kits

HEAD Blood Collection Kits

Total Number of Blood Collection Kits Requested
(same collection for BL, month 18)

Total Number of Blood Supplemental Kits Requested
Typically one per site per year

Total Number of Frozen Blood Shipping Kits Requested
Includes small frozen shipper

HEAD Frozen Shipping Kits

Total Number of Frozen Shipping Kits Requested
*For batch shipments of 5-6 cryoboxes

Do you require any individual supplies?

Yes

No

[reset](#)

Each Blood-Based Kit Includes:

1: Serum red top tube (10 ml)
5: EDTA (Lavender-Top) Blood Collection Tube (10 ml)
1: EDTA (Lavender-Top) Blood Collection Tube (6 ml)
3: 2ml Robotic Freezer Cryovials- RED
16: 2ml Robotic Freezer Cryovials - PURPLE
2: 2ml Robotic Freezer Cryovials - BLUE
5: 2ml Robotic Freezer Cryovials - GRAY
5: Disposable graduated transfer pipette (3ml)
1: 50ml conical Tube
7: Pre-printed Collection Tube Label
26: Cryovial Label
3: Pre-printed Kit Number Label

- Indicate the quantity needed of each kit
- Once selected, kit components of the chosen kit will appear at the bottom of the screen (Pictured)
- Click “Submit” to turn in your request.
- The IU staff will notify you that your request has been received and address any issues.
- ****Note: You can order more than one type of kit in a single kit request****

NCRAD Kit Request Module: When It Must be Used

- Each site will be responsible for ordering kits (labels included) and maintaining supplies on site for scheduled participants
- To order, sites will use the Indiana University online kit ordering module: <https://kits.iu.edu/head>
- Allow a minimum of **2-3 weeks** for your order to be processed and delivered.

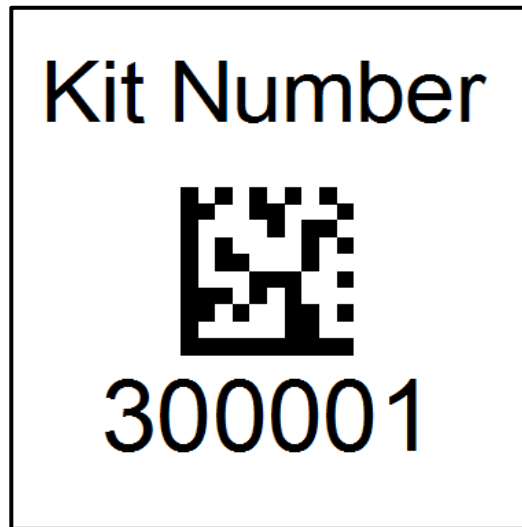
Specimen Labels



Label Type Summary

1. Kit Number Labels
2. HEAD ID Labels
3. Collection Tube Labels
 - Differ by specimen type
4. Cryovial Labels

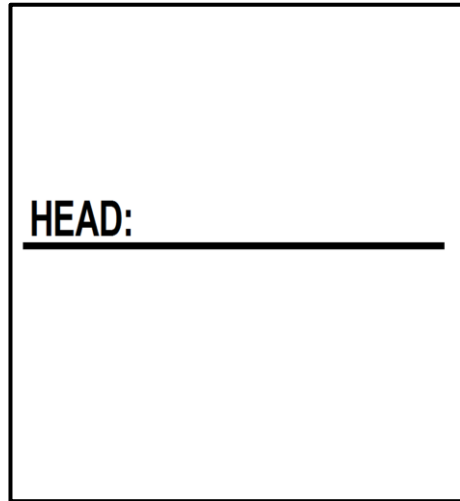
Kit Number Labels



- Used to track patient samples and provide quality assurance
- Will be placed on the following locations:
 1. Biological Sample and Shipment Notification Form
 2. Outside cryobox that houses aliquot tubes during storage and shipment

Provided by NCRAD in the kits

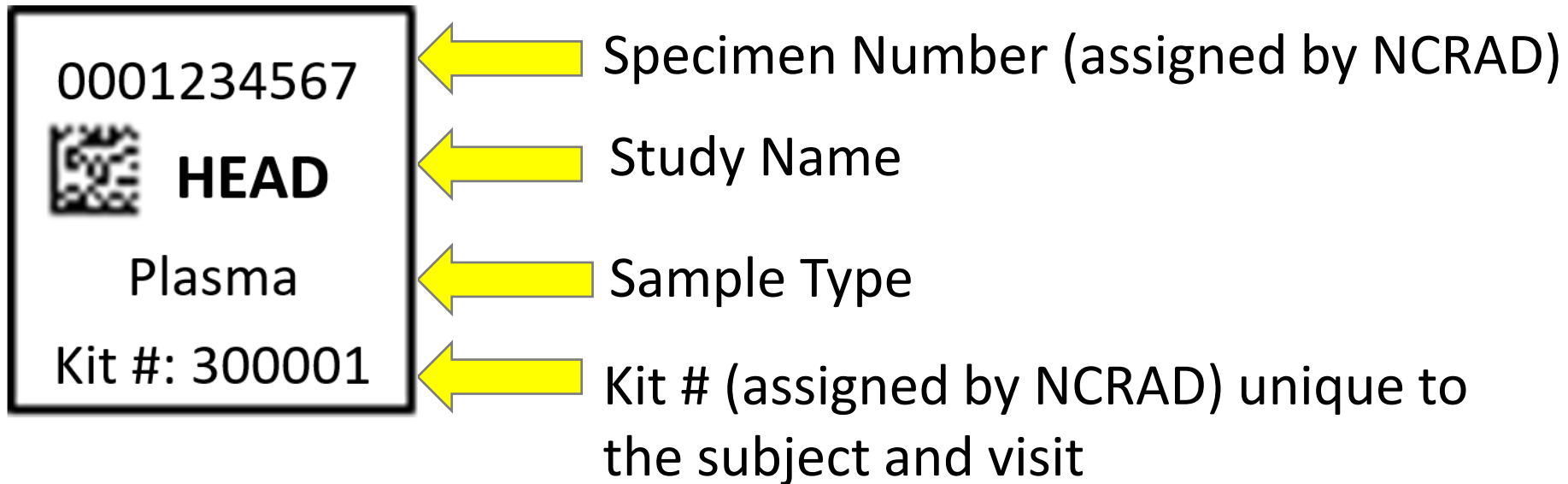
HEAD ID Label



HEAD:

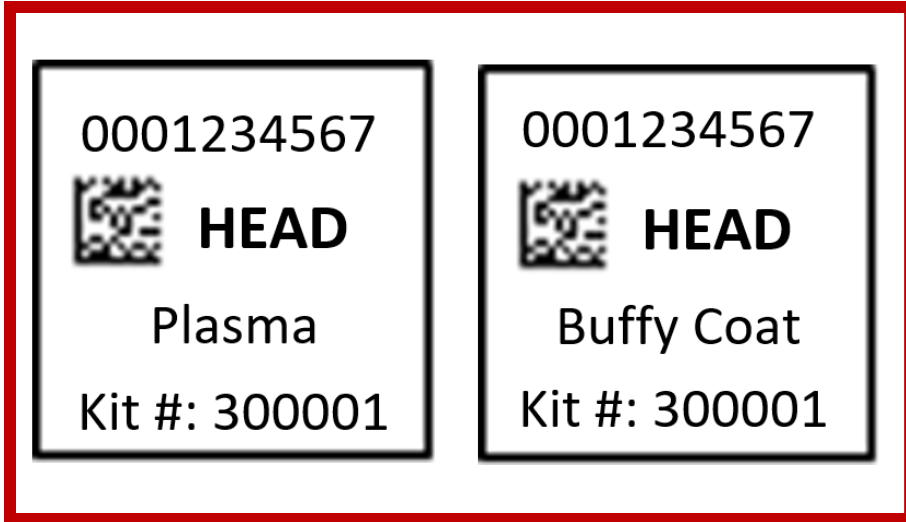
- Subjects will be identified by their HEAD ID
- The HEAD ID may only be available shortly before the visit
- Sites will be responsible for handwriting this onto the provided labels
 - Must use Fine point permanent marker

Collection Tube Labels

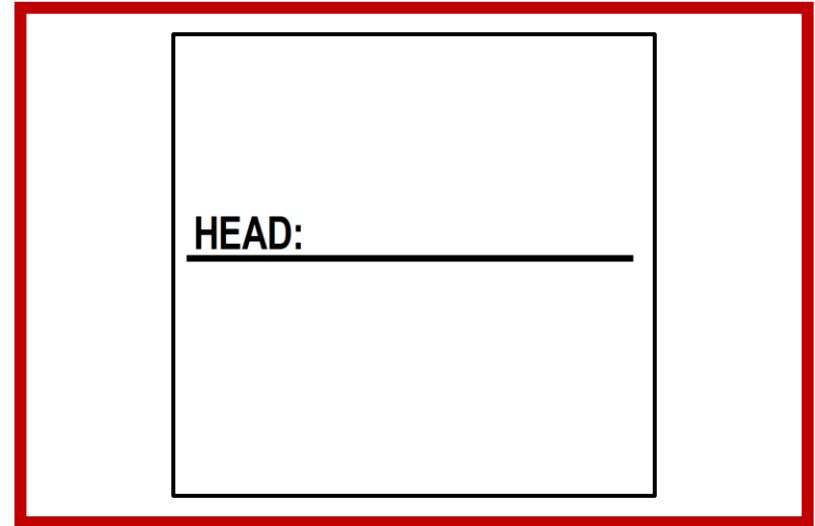


Collection Tubes - Blood

Label 1: Collection Tube Label

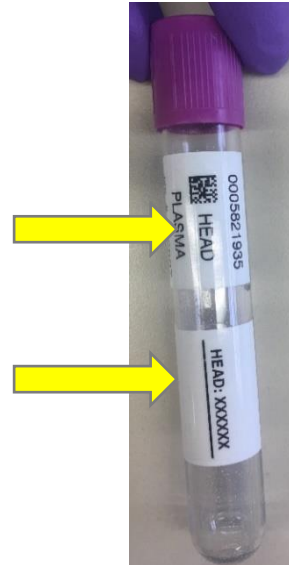


Label 2: HEAD ID Label



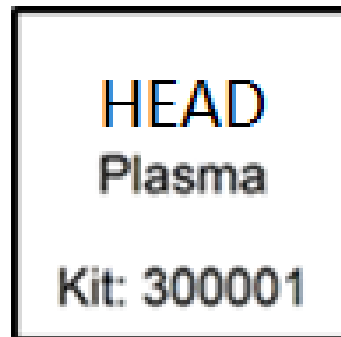
Collection/Aliquot
tube label
*place barcode
near top

HEAD ID label



- All collection tubes will have two labels
 - The Collection Tube Labels
 - The handwritten HEAD ID Label

Cryovial Tube Labels – Serum, Plasma and Buffy Coat

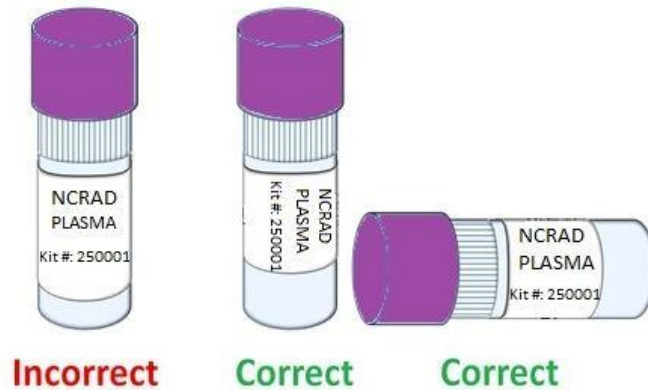


- Cryovial tube label only
- Please don't cover barcode on tube with label!

Labeling Biologic Samples

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.



Handling/Processing Study Specimens



Site Required Equipment





Blood Collection/Safety Equipment

1. PPE
 - Lab Coat, Safety Glasses
2. Tourniquet
3. Alcohol Prep Pad
4. Gauze Pad
5. Butterfly Needles
6. Bandage
7. Sharps Bin and Lid

Processing/Storage Equipment

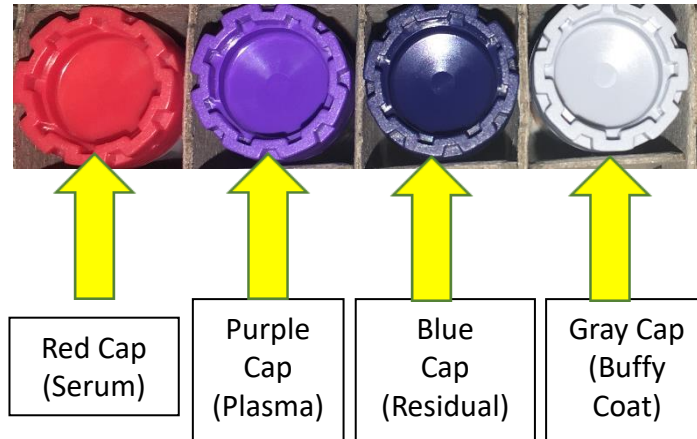
1. Centrifuge capable of ≥ 2000 rcf with refrigeration to 4°C
2. -80°C Freezer
3. Wet Ice Bucket

Sample Collection - Blood

Draw Tube Order	Tube Type	Number of Tubes Drawn	Tube Image
1	PAXgene™ Tube for RNA	1	
2	Serum (Red-Top) Tube (10 ml)	1	
3	EDTA (Lavender-Top) Tube (10ml)	5	
4	EDTA (Lavender-Top) Tube (6 ml)	1	

Aliquot Cap Colors

Cap Color	Sample Type
Red Cap	Serum
Purple Cap	Plasma
Blue Cap	Plasma Residual (<1.5ml) (Document Specimen Number and Volume of Residual Aliquot on Sample Form)
Gray Cap	Buffy Coat



RNA Preparation (2.5ml PAXgene™ Tube)



Step One



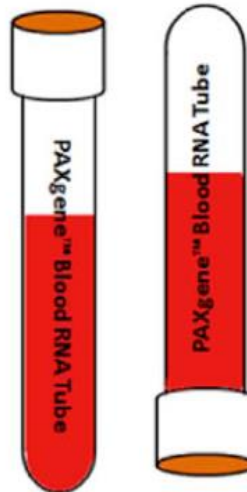
- Store tubes at room temperature.
- Label tubes with pre-printed labels prior to blood draw.

Step Two



- Collect blood in PAXgene™ tube allowing blood to flow for 10 seconds and ensuring blood flow has stopped.

Step Three



- Immediately after blood draw, invert tubes 8-10 times to mix samples.

Step Four



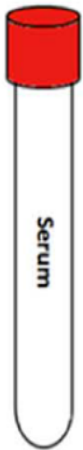
- Store tubes at -80°C in a wire rack until shipment.



Serum Preparation (10ml Red Top Tube)



Step One



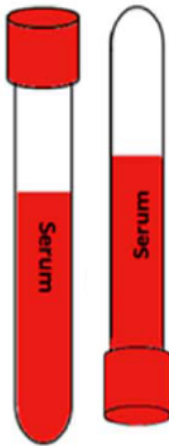
- Store tubes at room temperature.
- Label tubes and cryovials with pre-printed subject labels prior to blood draw.

Step Two



- Collect blood in Serum Tube allowing blood to flow for 10 seconds and ensuring blood flow has stopped.

Step Three



- Immediately after blood draw, invert tube 5 times to mix samples.

Step Four

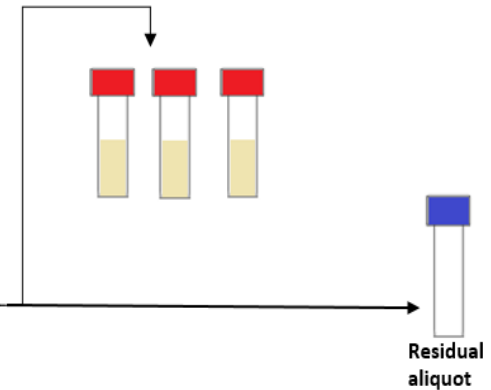


- Allow blood to clot for 30 minutes.
- Within 60 minutes of blood draw, centrifuge samples at 2000 x g for 10 minutes at 4°C.

Step Five



- Must be spun, aliquoted, and stored in -80°C freezer within 2 hours of collection.



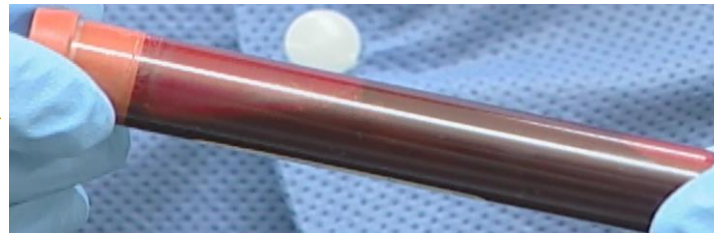
- Adhere preprinted labels to the red-cap cryovials.
- Aliquot 1.5 ml into each cryovial tube.
- If a residual aliquot is created, document specimen number and volume on Sample Notification Form.
- Store serum aliquots at -80°C until shipment.

Serum Tube (Serum Collection)



Serum Tube (unfilled)

** Please note: After standing at room temperature for 30 minutes, blood will be clotted and immobile**

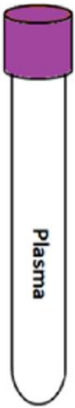


Serum Tube (after centrifuge)

Plasma and Buffy Coat Preparation (10ml Lavender-Top Tube x 5)



Step One



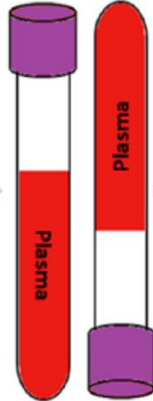
- Store tubes at room temperature.
- Label tubes with preprinted labels prior to blood draw.

Step Two



- Collect blood in EDTA Tubes allowing blood to flow for 10 seconds and ensuring blood flow has stopped.

Step Three



- Immediately after blood draw, invert tubes 8-10 times to mix samples.

Step Four



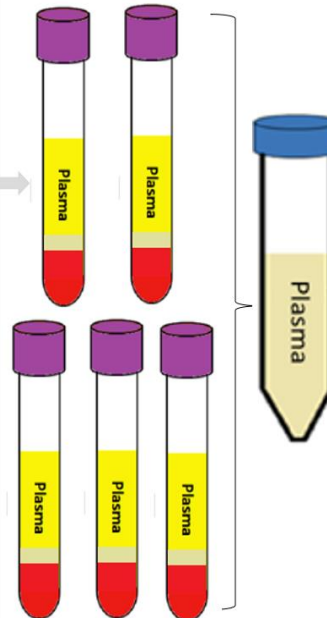
- Place thoroughly mixed tubes on wet ice until centrifugation begins.

Step Five



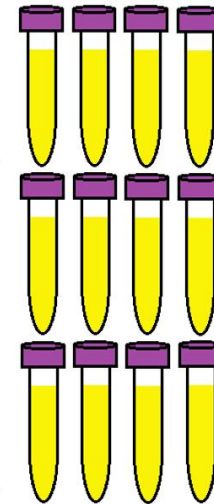
- Centrifuge samples at 2000 x g at 4°C for 10 minutes.
- Samples need to be spun, aliquoted, and in the freezer within 2 hours from the time of collection.

Step Six



- Pool all plasma from the 5 EDTA tubes into a 50ml conical tube and invert gently 3 times to mix the plasma.

Step Seven

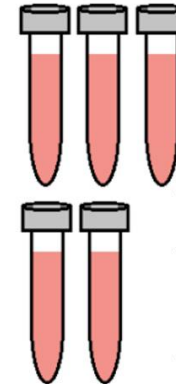


- Adhere preprinted labels to the purple cap cryovials.
- Aliquot 1.5 ml into each cryovial tube.
- If a residual aliquot is created, document specimen number and volume on Sample Notification Form.
- Store plasma aliquots at -80°C until shipment.



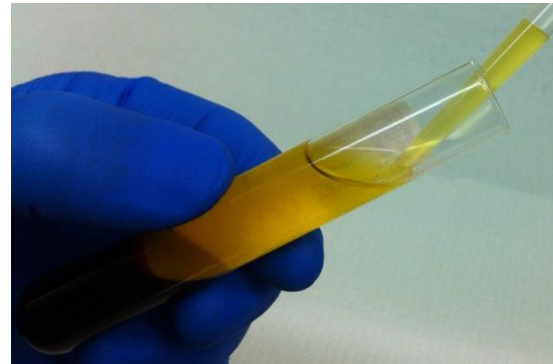
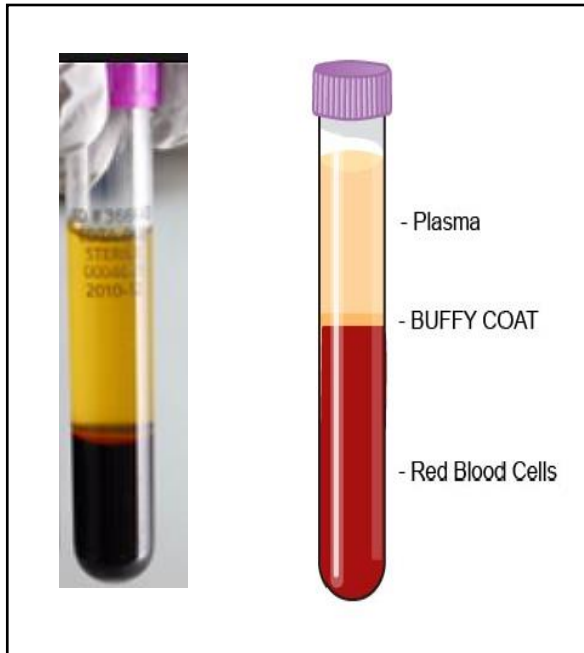
Residual aliquot

Step Eight

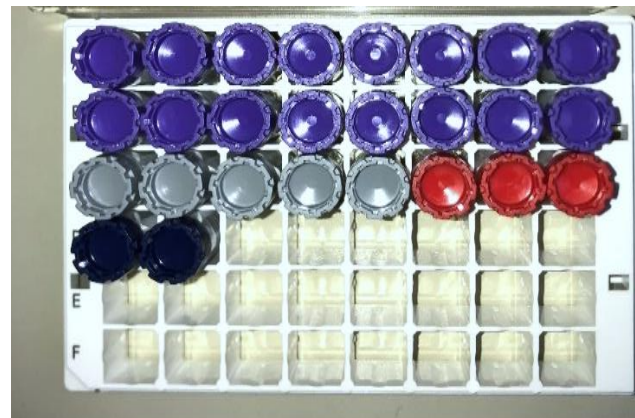


- Adhere preprinted labels to the gray cap cryovials.
- Using a clean pipette tip, collect the buffy coats (may have residual plasma and some RBCs included).
- Transfer the buffy coats into the cryovial tubes.
- Store buffy coat aliquots at -80°C until shipment.

EDTA Tube (Plasma Collection)

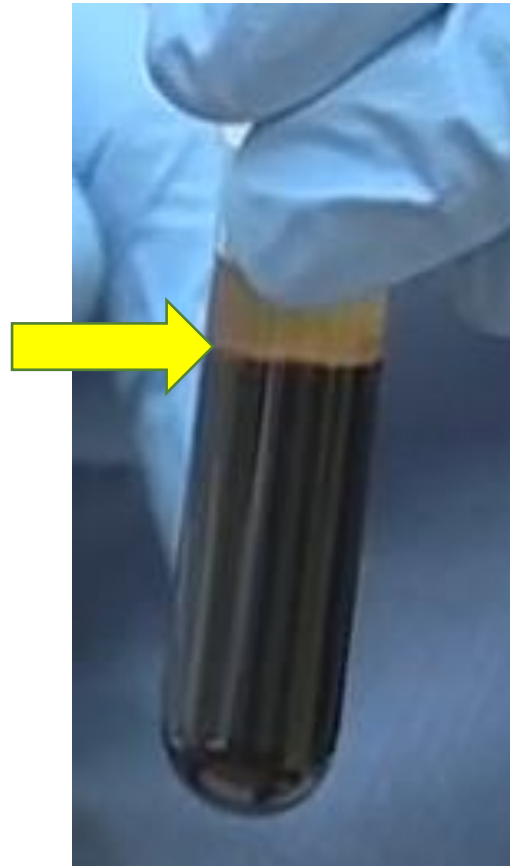


Plasma Aliquots
(up to 17 possible)



Close up view of 2.0 ml
cryovial

EDTA Tube (Buffy Coat Collection)



Important Note:

- ❖ Buffy Coat aliquots will be distinguished from the plasma aliquots through a gray cap.

Whole Blood Preparation (6 mL Lavender-Top Tube)



Step One



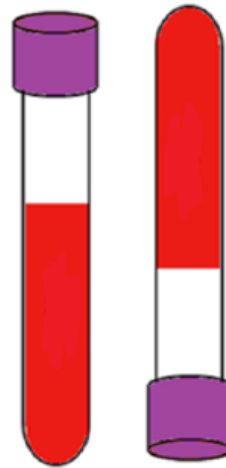
- Store tubes at room temperature.
- Label tubes with pre-printed subject labels prior to blood draw.

Step Two



- Collect blood in tube allowing blood to flow for 10 seconds and ensuring blood flow has stopped.

Step Three



- Immediately after blood draw, invert tube 3 times to mix sample.

Step Four



- Immediately after inversion, freeze the sample in an -80°C freezer until ready to ship.



Sample Shipping



Blood Sample Shipment Summary

Draw Tube Order	Sample Type	Tube Type	Tubes to NCRAD	Ship
1	Whole blood for transcriptome analysis	PAXgene™ Blood RNA Collection Tube (2.5 ml) for RNA	1	Frozen
2	Whole blood for isolation for serum	SERUM: 2.0 ml cryovials with red cap (residual volume placed in 2.0 ml cryovial with blue cap)	Up to 4	Frozen
3	Whole blood for isolation of plasma & buffy coat (for DNA extraction)	PLASMA: 2.0 ml cryovials with purple cap (residual volume placed in 2.0 ml cryovial with blue cap)	Up to 17	Frozen
		BUFFY COAT: 2.0 ml cryovial	5	Frozen
4	Whole blood for future analysis	EDTA (Lavender-Top) Blood Collection Tube (6 ml)	1	Frozen

Frozen Sample Shipping

- **Ship Monday-Wednesday Only**
 - Plasma
 - Buffy Coat
 - Serum
 - Whole Blood for RNA
- Hold packaged samples in a -80°C freezer until pickup.
- Batch Samples together
 - 5 cryoboxes
 - Batch shipping should be performed quarterly or as a full shipment of specimens accumulates, **whichever is sooner.**

Frozen Shipping - Cryoboxes



Place frozen RNA
(and frozen EDTA
(6ml) tube, when
applicable) in
bubble wrap tube
sleeves.

Place cryobox in one
Biohazard Bag.

Shipping Frozen Samples

- Schedule UPS
- *Send Biological Sample and Shipment Notification Form to IU (US) ahead of shipment*
 - *Email: alzstudy@iu.edu*

Frozen Shipping – Dry Ice Requirements



- Fully cover the cryoboxes with about 2 inches of dry ice in the provided shipper.
- Each Styrofoam shipper must contain about 45 lbs (20 kg) of dry ice.

Frozen Shipping – Dry Ice Requirements

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



UPS ShipExec System

- Log into the ShipExec Thin Client at <https://kits.iu.edu/ups>
 - If a new user or contact needs access, please reach out to your study contact for access
- Follow instructions on section 8.2 of HEAD Manual of Procedures to create your return airbill and schedule a UPS pickup

Shipping Regulations and Training

PLEASE NOTE:

- All study personnel responsible for shipping should be certified in biospecimen shipping.
- It is the responsibility of each site to ensure that the appropriate training has been provided and conducted in regards to IATA shipping.

UN3373 Biological Substance, Category B Training

- Biological Substance, Category B are specimens being transported for “investigational purposes”
- Recommend: investigator sites document training of category B/dangerous goods
- We recommend establishing a record of your staff’s training and date of instruction
- The training records must be made available upon request by the appropriate national authority
 - Additional information from the Department of Transportation (DOT) can be found on their website <http://hazmat.dot.gov>

Biological Sample and Shipment Notification Forms

- A copy of the sample form *must* be emailed to NCRAD prior to the date of sample arrival.
- Please include sample forms in all shipments of frozen and ambient samples.
- Email: alzstudy@iu.edu



Biological Sample Notification Form- Blood



Appendix B: Biological Sample and Shipment Notification Form

Please email the form on or prior to the date of shipment.

To: Diont'e Keys Email: alzstudy@iu.edu Phone: 1-800-526-2839

General Information:	Tracking #: _____
From: _____	Date: _____
Phone: _____	Email: _____

Study: HEAD Visit (circle one): BASELINE 18M	KIT BARCODE
Site ID: _____ PTID: _____	
Sex (circle one): M F Year of Birth: _____	

Blood Collection:			
Date Drawn: _____ [MMDDYY]	Time of Draw: _____ [HHMM]		
Last date subject ate: _____ [MMDDYY]	Last time subject ate: _____ [HHMM]		
Lavender Top Whole Blood Tube (6 ml)		RNA (PAXgene™ Tube)	
Original volume drawn: _____ mL	Time EDTA tube placed in freezer: _____ [HHMM]	Original volume drawn: _____ mL	Time PAXgene™ tube placed in freezer: _____ [HHMM]

Blood Processing:			
Serum (Red-top) Tube (10 mL)			
Time spin started: _____ [HHMM]	Number of 1.5 mL serum aliquots created (red cap): _____		
Duration of centrifuge: _____ Minutes	If applicable, volume of residual serum aliquot (less than 1.5 mL in blue cap): _____ mL		
Temp of Centrifuge: _____ °C	Rate of centrifuge: _____ x g	If applicable, specimen number of residual serum aliquot (last four digits): _____	
Original volume drawn: _____ mL	Time aliquots placed in freezer: _____ [HHMM]		
Time aliquoted: _____ [HHMM]	Storage temperature in freezer: _____ °C		

Plasma & Buffy Coat (Lavender-top) Tube (10 mL)			
Time spin started: _____ [HHMM]	Rate of centrifuge: _____ x g		
Duration of centrifuge: _____ Minutes	Time aliquoted: _____ [HHMM]		
Temp of Centrifuge: _____ °C	Number of 1.5 mL plasma aliquots created (purple cap): _____ x 1.5 mL		
Original volume drawn - EDTA #1 _____ mL	If applicable, volume of residual plasma aliquot (less than 1.5 mL in blue cap): _____ mL		
Original volume drawn - EDTA #2 _____ mL	If applicable, specimen number of residual plasma aliquot (Last four digits): _____		
Original volume drawn - EDTA #3 _____ mL	Time aliquots placed in freezer: _____ [HHMM]		
Original volume drawn - EDTA #4 _____ mL	Storage temperature in freezer: _____ °C		
Original volume drawn - EDTA #5 _____ mL			
Aliquot volume – Buffy coat #1 _____ mL	Buffy coat aliquot #1 (last four digits): _____		
Aliquot volume – Buffy coat #2 _____ mL	Buffy coat aliquot #2 (last four digits): _____		
Aliquot volume – Buffy coat #3 _____ mL	Buffy coat aliquot #3 (last four digits): _____		
Aliquot volume – Buffy coat #4 _____ mL	Buffy coat aliquot #4 (last four digits): _____		
Aliquot volume – Buffy coat #5 _____ mL	Buffy coat aliquot #5 (last four digits): _____		

Notes: _____

Blood collected for:

- Serum
- Plasma
- Buffy Coat/DNA
- Whole blood banking
- Whole Blood for RNA

Send by E-mail and include a copy in each shipment

NCRAD Website

Helpful Pages



- https://ncrad.org/holiday_closures.html
- https://ncrad.org/friday_blood_draws.html

What to do for Friday Blood Draws

NCRAD is not open for business on Saturday or Sunday; therefore, we ask that no samples be shipped on a Friday. We cannot guarantee the conditions in which the samples will be held by the shipping courier over the weekend. It is important to have plans in place for each type of sample to be held over the weekend prior to shipping. Please refer to the table below for how to handle samples drawn on a Friday.

When possible, please only ship frozen samples on Monday-Wednesday. There is always the potential for an unexpected shipping courier delay and by shipping Monday through Wednesday there should be enough time to receive the samples before the weekend.

Sample Type	Tube Type	Product	Shipment Method	Friday Draw Instructions
Plasma	Polypropylene Aliquot Tubes	Plasma	Frozen	Plasma must be processed and aliquoted locally the day of collection. Once aliquoted, samples are stored upright in a -80°C freezer before shipment. The aliquots may then be packed with dry ice pellets and shipped frozen as the study MOP dictates.
Buffy Coat	Polypropylene Aliquot Tubes	DNA	Frozen	Buffy Coat aliquots must be processed and aliquoted locally the day of collection. Once aliquoted, the sample must then be transferred into a -80°C freezer until shipment. The aliquot may then be packed with dry ice pellets and shipped frozen as the study MOP dictates.

Holiday 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

HEAD Active Study Page

HEAD Active Study Page



Welcome HEAD Study staff, coordinators, and PI's.

This section encompasses study specific tools and videos for your reference. If you have any questions, comments, or new ideas please contact NCRAD by email or phone (800) 526-2839 or directly at (317) 278-1170.

HEAD Biospecimen Collection Schedule

	Baseline	18 Month
Serum	✓	✓
Plasma	✓	✓
DNA	✓	✓
Whole Blood for banking	✓	✓
Whole Blood for RNA**	✓	✓

**2.5 ml PAXgene™ RNA Tube for Whole Blood.



BANK SAMPLES
with NCRAD



SAMPLE TYPES
we Bank

Download Documents

[Blood Sample Form](#)

Additional Resources

[Kit Request System](#)

[Friday Blood Draws](#)

[Shipping Address](#)

[Holiday Closures](#)

Questions/Comments

Email: alzstudy@iu.edu

Phone: 800-526-2839

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