

Cerebral Autosomal Dominant Arteriopathy with Sub-cortical Infarcts and Leukoencephalopathy Study

COLLECTION AND SHIPMENT TRAINING
Version 1.1



Training Overview

- Contact Information
- Collection Schedule
- Kit Request Module
 - Specimen Labels
- Handling/Processing Study Specimens
- Incomplete or Difficult Blood Draws and Redraws
 - Packaging Sample Shipments
 - Sample Form
 - NCRAD Website
 - Common Nonconformance Issues
 - Questions?



NCRAD Contact Information

Questions?

Zoë Potter, BA, CCRP, Study Coordinator

Phone: (317) 278-9086

Email: zdpotter@iu.edu

General NCRAD Contact Information

Phone: 1-800-526-2839

Email: alzstudy@iu.edu

Website: www.ncrad.org

CADASIL Study Specific Webpage: NCRAD - CADASIL Active Study Page



CADASIL Blood-Based Collection Schedule

	Visit 1 (Baseline)	Visit 2 (18 month)	Visit 3 (36 month)
Plasma	X	X	X
Buffy Coat	X	X	X
RNA	X	X	X
Serum	X	X	X



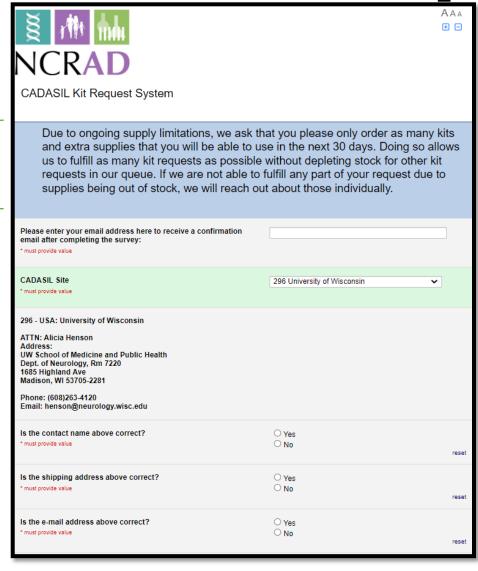
Kit Request Module

http://kits.iu.edu/cadasil



CADASIL Kit Request Module

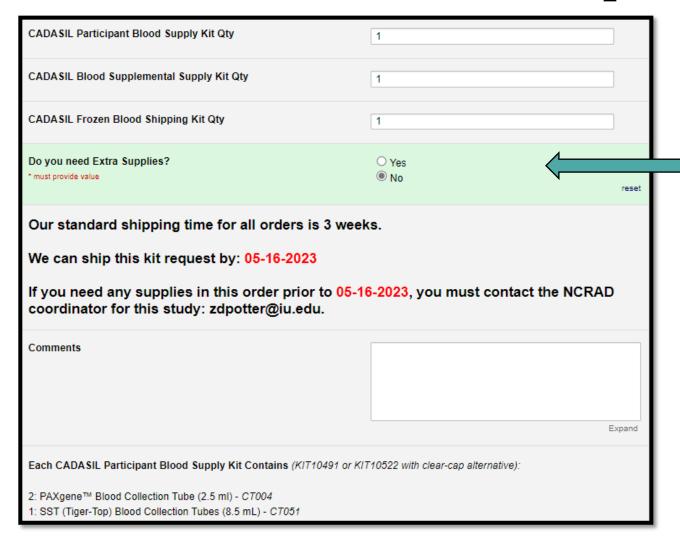
If possible, only order what you will need in the next month



- Enter your email to receive a confirmation email after you submit your kit request.
- Choose your site from the drop-down list.
- The coordinator name and contact information will appear.
- Verify that this information is accurate. Correct if necessary.



CADASIL Kit Request Module



- Indicate the quantity needed of each kit
 - Once selected, kit components of the chosen kit will appear at the bottom of the screen
- You can order extra supplies individually by selecting "Yes" here.
- We will return requests within 3 weeks from the order date.
 - If you need any supplies expedited, please contact the NCRAD Coordinator via email.
- Click "Submit" to turn in your request.
- **Note: You can order more than one type of kit in a single kit request**



CADASIL Kit List

- CADASIL Participant Blood Supply Kit
- CADASIL Blood Supplemental Supply Kit
- CADASIL Frozen Blood Shipping Kit

• Each individual site will be responsible for ordering and maintaining a steady supply of kits from NCRAD. We advise sites to keep a supply of each kit type available for scheduled participants.

• Be sure to check your supplies and order additional materials before you run out or supplies expire so you are prepared for study visits.

• Allow a minimum of 3 weeks for your order to be processed and delivered.

• Due to ongoing supply limitations, we ask that you please only order as many kits and extra supplies that you will be able to use in the next 30 days.

Specimen Labels

Provided by NCRAD



Four Label Types

Kit Number

426534

Kit Number

Labels

CADASIL
0042961830
PLASMA
Kit #: 458451
Collection Tube
Labels

Site ID:

PTID: CC

Site and CADASIL
ID Labels

CADASIL
Plasma
Kit # 422430

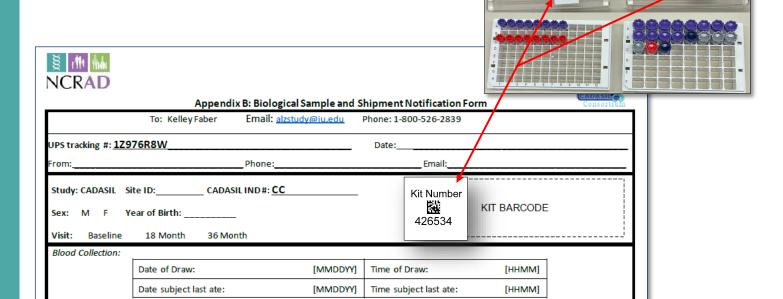
Cryovial Tube
Labels



Kit Number Labels

Kit Number
426534

- Used to track patient samples and provide quality assurance – Will be placed on the following locations:
 - 1. Blood Sample and Shipment Notification Form (Appendix B).
 - 2. Lid of cryobox that houses aliquot tubes during storage and shipment.
 - 3. One extra label provided



Collection Tube Labels







- Collection Tube labels have 4 components:
 - Study name
 - 10-digit specimen barcode
 - Specimen type
 - Kit number
- Will be placed on the following locations :
 - All Collection Tubes
 - 4 x EDTA (Lavender-Top) Blood Collection Tube (10 mL)
 - 2 x PAXgene[™] Blood Collection Tube (2.5 mL)
 - 1 x SST (Tiger-Top) Blood Collection Tube (8.5 mL)

Site and CADASIL ID Labels

Site ID:

PTID: CC

- Subjects will be identified by their Site and PTID
- Sites will be responsible for handwriting this onto the provided labels
 - Must use fine point permanent marker
 - Write information on label prior to adhering to tube
- Will be placed on the following locations :
 - 4 x EDTA (Lavender-Top) Blood Collection Tube (10 mL)
 - 2 x PAXgene™ Blood Collection Tube (2.5 mL)
 - 1 x SST (Tiger-Top) Blood Collection Tube (8.5 mL)

Cryovial Tube Labels

CADASIL Plasma Kit # 422430 CADASIL Buffy Coat Kit # 422430

CADASIL Serum Kit # 422430

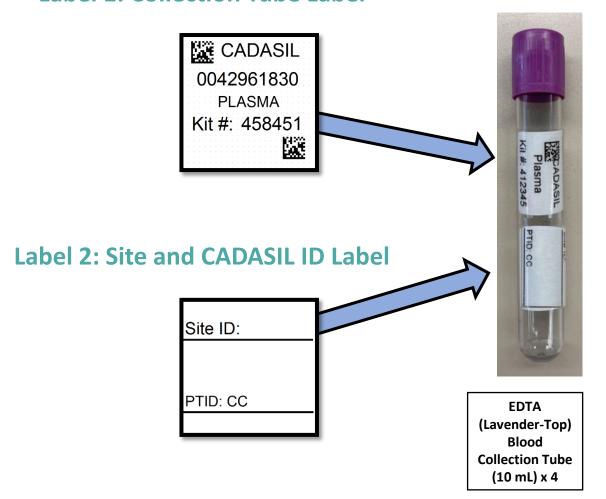
- Only one label to be placed on each 2.0 mL cryovial
 - Plasma
 - From EDTA tube
 - Buffy Coat
 - From EDTA tube
 - Serum
 - From SST tube

Important: Do not cover barcode that is pre-etched on cryovial.



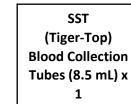
Blood Collection Tube Labels:

Label 1: Collection Tube Label







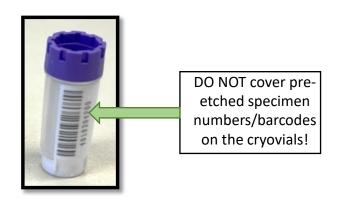


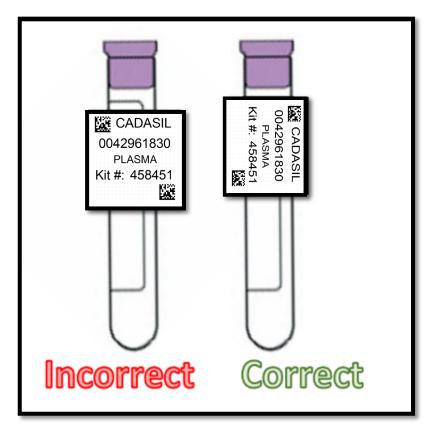


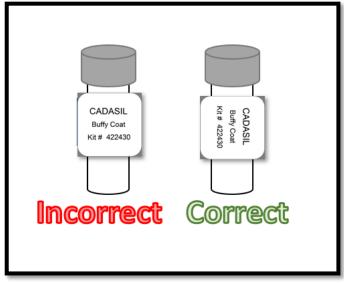
PAXgeneTM Blood Collection Tube (2.5 mL) x 2

Labeling Biologic Samples

- Label all collection and aliquot tubes
 <u>before</u> cooling, collecting, processing or freezing samples
- •Label only <u>1</u> subject's tubes at a time to avoid mix-ups
- •Wrap the label around the tube <u>horizontally</u>. Label position is important for <u>all</u> 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) Personal Protective Equipment:
 - 1) Lab coat, nitrile/latex gloves, safety glasses
- 2) Tourniquet
- 3) Alcohol Prep Pad
- 4) Gauze Pad
- 5) Bandage
- 6) Butterfly needles and hub
- 7) Microcentrifuge tube rack
- 8) Sharps bin and lid

PROCESSING/STORAGE EQUIPMENT

- Centrifuge capable of ≥ 2000 x g at <u>room temperature</u>
- 2) -80°C Freezer
- 3) Wet Ice Bucket



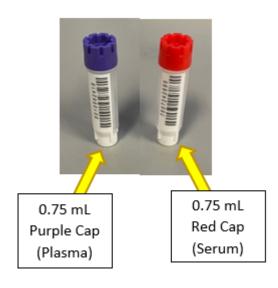
Blood Draw Order

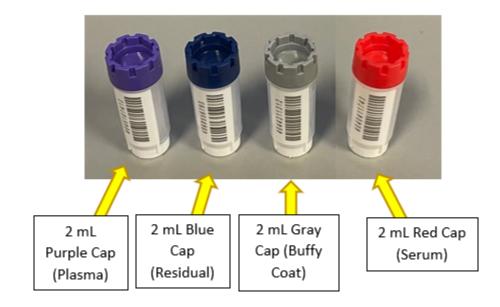
Tube Type	Number of Tubes Drawn	Tube Image	
1. EDTA (Lavender-Top) Blood Collection Tube (10 mL)	4	Plasma Kit #: 412345	
2. PAXgene [™] Blood Collection Tube (2.5 mL)	2	RNA Kit #: 412345 PTID: CC	
3. SST (Tiger-Top) Blood Collection Tubes (8.5 mL)	1	00042127380 PTID: CC	



Aliquot Cap Colors

Cap Color	Sample Type	
Purple Cap (8 x 0.75 mL and 12 x 2 mL)	Plasma	
Blue Cap (2 x 2.0 mL)	Residual (plasma and serum)	
Gray Cap (4 x 2.0 mL)	Buffy Coat	
Red Cap (8 x 0.75 mL and 1 x 2 mL)	Serum	

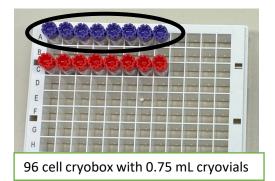


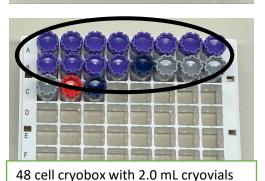




Plasma Collection

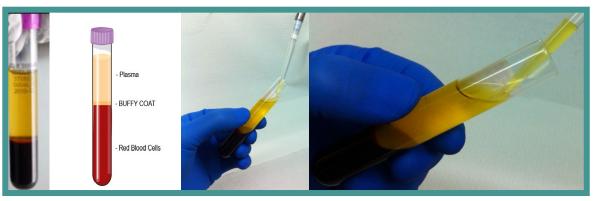






4 x EDTA (Lavender-Top) Blood Collection Tube (10 mL)

- Create up to (8) 0.25 mL plasma aliquots
- Create up to (12) 1.5 mL plasma aliquots
- Create up to (1) 1.5 mL residual plasma aliquot

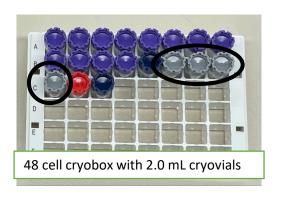


NOTE: When pipetting plasma from the conical into the cryovials, be very careful to pipette the plasma top layer only, leaving the buffy coat and the red blood cell layers untouched.



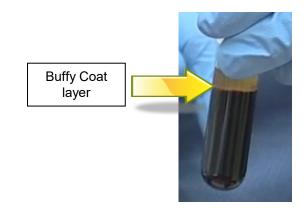
Buffy Coat Collection





4 x EDTA (Lavender-Top) Blood Collection Tube (10 mL)

- Create up to (4) 1.5 mL buffy coat aliquots
 - Expected to have a reddish color from the RBCs.
 - Be sure to only place the buffy coat from one EDTA tube into each cryovial

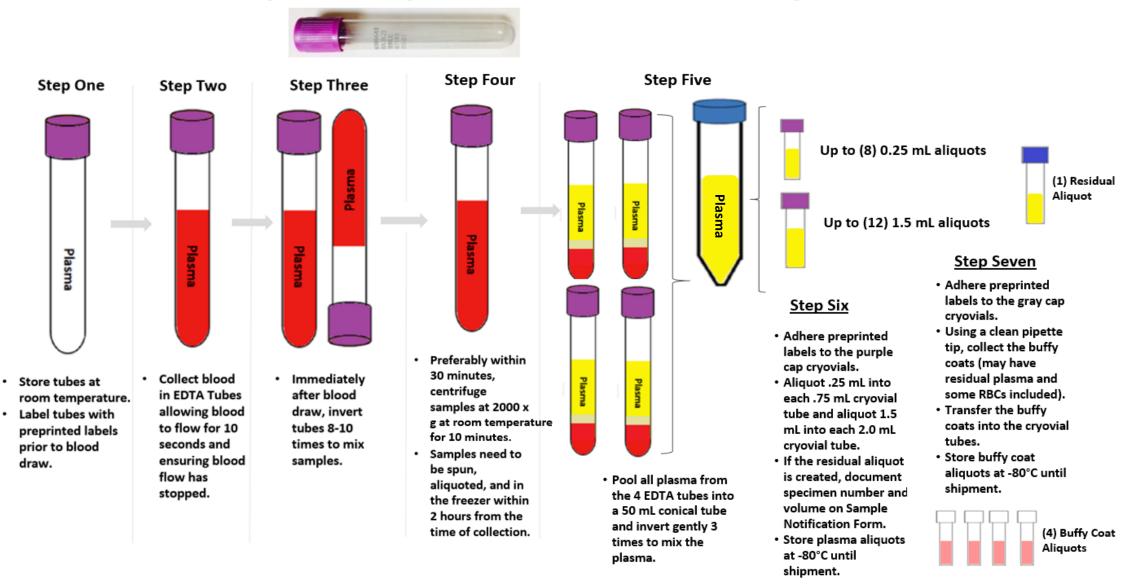








Plasma and Buffy Coat Preparation (10ml Lavender-Top Tube X 4)



RNA Collection

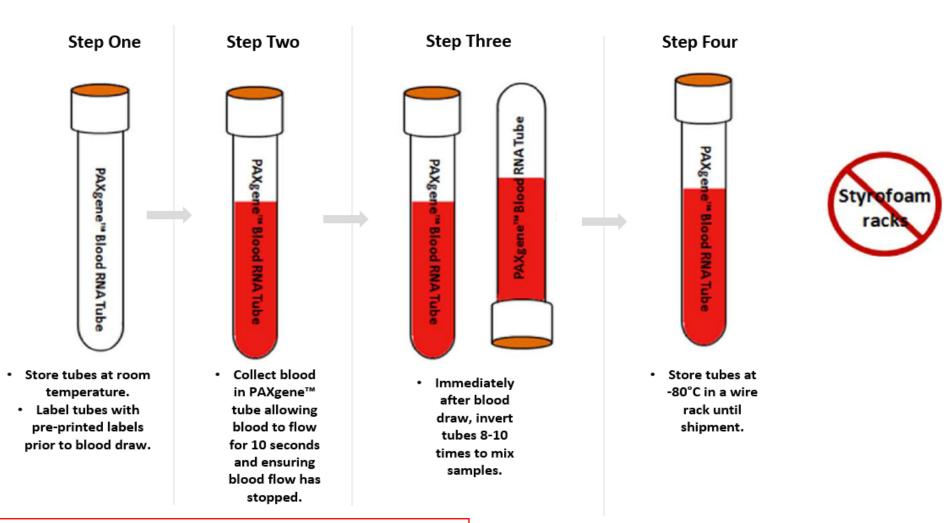


- 2 x PAXgene™ Blood Collection Tube (2.5 mL)
 - Both tubes are to be shipped to NCRAD frozen, without processing at the collection site.



RNA Preparation (2.5ml PAXgene™ Tube)

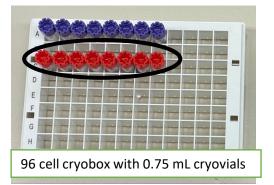


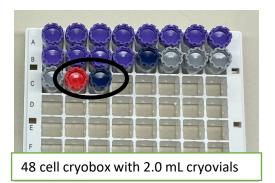




Serum Collection

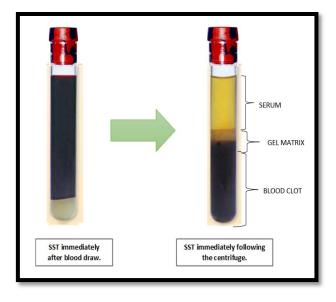






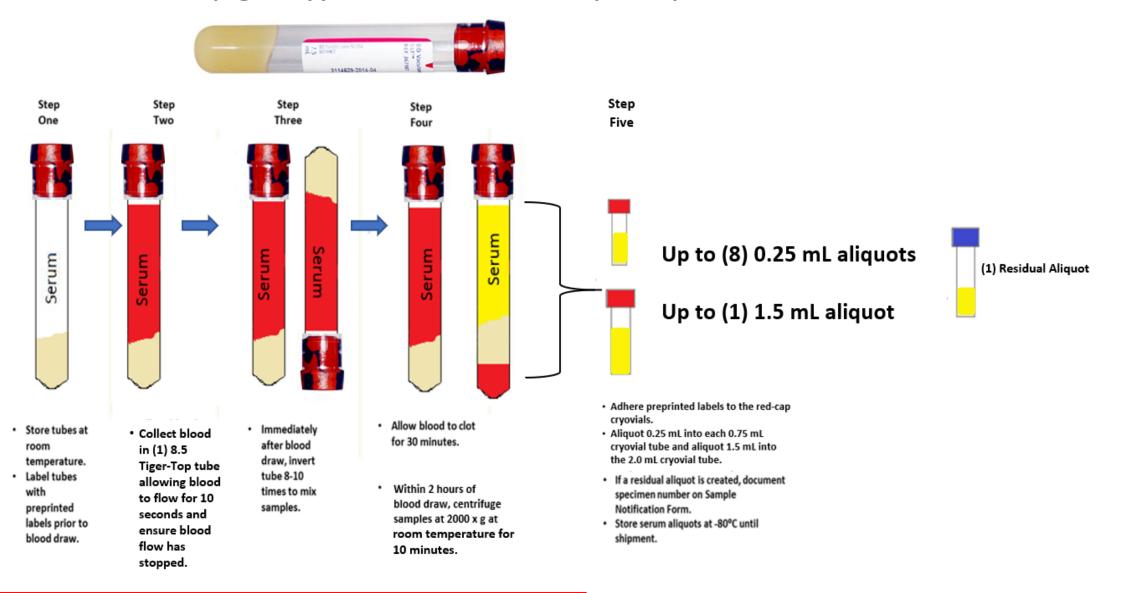
1 x SST (Tiger-Top) Blood Collection Tubes (8.5 mL)

- Create up to (8) 0.25 mL serum aliquots
- Create up to (1) 1.5 mL serum aliquots
- Create up to (1) 1.5 mL residual serum aliquot





SST (Tiger-Top) Blood Collection Tubes (8.5 mL) for Serum x 1



Incomplete or Difficult Blood Draws and Redraws

Important Note

If challenges arise during the blood draw process, it is advised that the phlebotomist discontinue the draw. Attempt to process and submit any blood-based specimens that have already been collected to NCRAD.

Redraws will be scheduled for samples submitted to NCRAD.



Situations may arise that prevent study coordinators from obtaining the total amount scheduled for biofluids. In these situations, please follow the below steps:

- 1. If the biofluids at a scheduled visit are partially collected:
 - a. Attempt to process and submit any samples that were able to be collected during the visit.
 - b. Document difficulties on the 'Biological Sample and Shipment Notification Form' prior to submission to NCRAD.
 - i. Indicate blood draw difficulties at the bottom of the 'Biological Sample and Shipment Notification Form' within the "Notes" section.
 - ii. Complete the 'Biological Sample and Shipment Notification Form' with tube volume approximations and number of aliquots created.
 - c. Contact a NCRAD coordinator and alert them of the challenging blood draw.
- 2. If the biofluids at a scheduled visit are not collected:
 - a. Contact the CADASIL Global Coordinator and a NCRAD coordinator to alert them of the challenging blood draw or circumstances as to why biofluids were not collected.
 - b. Schedule participant for a re-draw visit as quickly as possible.



Packaging Sample Shipments



Sample Shipment Summary

Sample Type	Tube Type	Number of Tubes Supplied in Kit	Processing/Aliquoting	Tubes to NCRAD	Ship	
Whole blood for isolation of plasma & buffy coat (for DNA extraction)	EDTA (Lavender-Top) Blood Collection Tube (10 mL)	4	N/A	N/A	N/A	
	PLASMA: 0.75 mL cryovials	8	0.25 mL plasma aliquot per 0.75 mL cryovial (Micronic™ purple cap)	8		
	PLASMA: 2.0 mL cryovials	12	1.5 mL plasma aliquot per 2.0 mL cryovial (Micronic™ purple cap)	12	Frozen	
	PLASMA RESIDUAL: 2.0 mL cryovials	1	1.5 mL plasma aliquot per 2.0 mL cryovial (Micronic™ blue cap)	1		
	BUFFY COAT: 2.0 mL cryovials	4	1 mL buffy coat aliquot per 2.0 mL cryovial (Micronic™ gray cap)	4		
Whole blood for RNA extraction	PAXgene [™] Blood Collection Tube (2.5 mL)	2	N/A	2	Frozen	
Whole blood for isolation of serum	SST (Tiger-Top) Blood Collection Tubes (8.5 mL)	1	N/A	N/A	N/A	
	SERUM: 0.75 mL cryovials	8	0.25 mL serum aliquot per 0.75 mL cryovial (Micronic™ red cap)	8		
	SERUM: 2.0 mL cryovials	1	1.5 mL serum aliquot per 2.0 mL cryovial (Micronic™ red cap)	1	Frozen	
	SERUM RESIDUAL: 2.0 mL cryovials	1	1.5 mL serum aliquot per 2.0 mL cryovial (Micronic™ blue cap)	1		



Frozen Shipment Packaging



All samples shipped frozen to NCRAD Monday-Wednesday ONLY



On the day of scheduled UPS pick-up, begin packaging specimens on dry ice at least 1 hour before UPS arrives. Hold samples in -80°C freezer until it is time to package the specimens on dry ice for shipment to NCRAD.



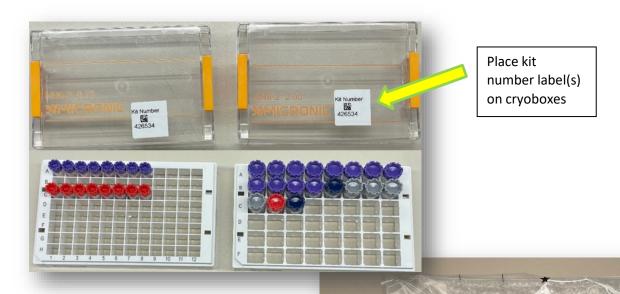
Include copy of Blood Sample Shipment and Notification Form



Batch shipping should be performed every (3) three months or when specimens from 4 participants accumulate, whichever is sooner.

Frozen Shipment Packaging

- Place all frozen labeled aliquots of plasma, buffy coat, serum, and residual aliquots from the same subject in the cryoboxes.
 Place both cryoboxes from the same subject into the biohazard bag with absorbent sheet.
- Place frozen (2) PAXgene™
 tubes in provided bubble wrap
 tube sleeves, seal, and place in
 biohazard bag with cryoboxes.
 Seal biohazard bag according to
 the instructions on the bag.





Specimen Transport Bag

Frozen Shipment Packaging

- Place 2-3 inches of dry ice in the bottom of the Styrofoam shipping container, then insert the cryoboxes laying upright.
- 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.
- Fill shipper to the top with dry ice!

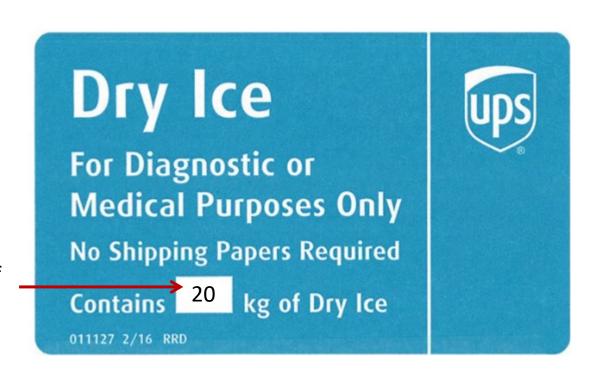




Frozen Shipping – Dry Ice Requirements

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

Net weight of dry ice in **kg**





Creating Airbills/Scheduling Pickups



UPS ShipExecTM Thin Client Website



Log into the ShipExec Thin Client: https://kits.iu.edu/UPS



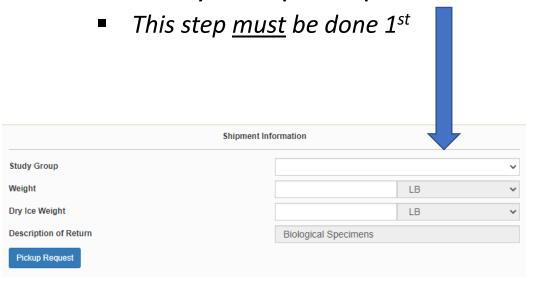
Click on the "Shipping" dropdown and click on "Shipping and Rating"





Finding Your Contact Information

On the right side of the screen, choose the name of your study from the "Study Group" drop down menu



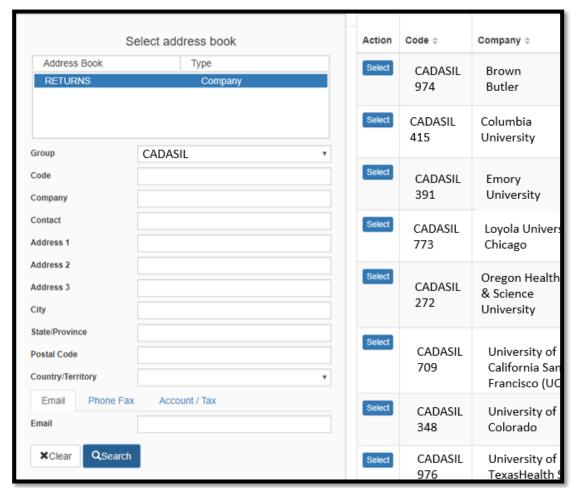
 On the left side of the screen, Click on the magnifying glass icon





Finding Your Contact Information

- On the right side of the screen, a list of all the site addresses within the study you selected should populate
- User can filter the search for their address further by filling in the "Company", "Contact", or "Address 1" fields
- Hit "Search" when ready.
- Once you have found your site address, click on the "Select" button to the left of the address
- If any information needs to be updated, please reach out to the NCRAD Coordinator of your study





Verify Information

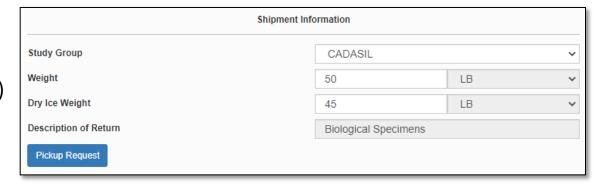
Please verify that both the shipping information AND study reference are correct for this shipment

	Ship From	Shipment Information					
		Study Group	CADASIL	~			
Q	Clear	Weight	50	LB v			
Code	CADASIL 296	Dry Ice Weight	45	LB 🗸			
Company	UW School of Medicine and Public Health	Description of Return	Biological Specimens				
Contact	Alicia Henson	Pickup Request	J 1				
Address 1	600 Highland Ave.	Tionup Request					
Address 2	K4354						
Address 3	Department of Neurology						
City	Madison						
State/Province	WI						
Postal Code	53792						
Country/Territory	United States 🗸						



Entering Shipment Information

- Frozen shipments
 - Enter the total weight of your package in the "Weight" field
 - Enter the dry ice weight in the "Dry Ice Weight" field
 - The "Dry Ice Weight" field cannot be higher than the "Weight" field (will receive an error message)





Need to request UPS Pickup?

- Click on the "Pickup Request" button
- Fill out all fields for the pickup request
- Enter in the "Earliest Time Ready" and "Latest Time Ready" in 24-hour format
 - Users must schedule pickup minimum 1 hour before "Earliest Time Ready"
- Choose a name and number that is the best to contact if the UPS driver has questions related to picking up your package
- Entering the Room Number and Floor will help the UPS driver locate your package
 - Room number field is free text
 - Floor field is numerical only
- Hit "Save" when done

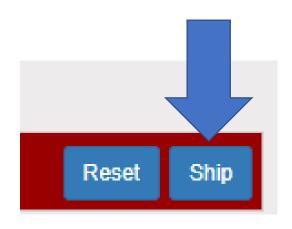


Create Pickup Request	×	
Pickup Date	2023-04-27	
Earliest Time Ready	17:00	
Latest Time Ready	21:00	
Contact Name	John Smith	ı
Contact Phone	555-555-5555	ı
Payment Method	Pay by shipper account	ı
Room Number	718	211
Floor	7	SIL
	Save	al



Shipping Packages

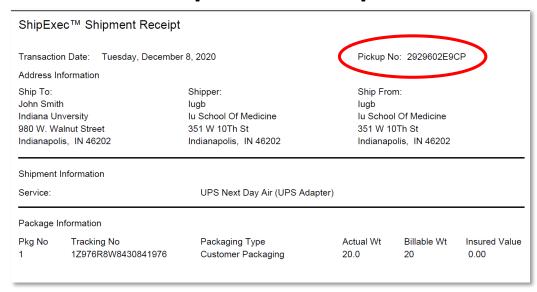
■ If all fields in "Ship From" and "Shipment Information" fields are completed, and pickup request is completed (if necessary), click Ship in the bottom right corner of the page





Accessing Airbill

Shipment Receipt



Check Pickup Status by going to UPS.com, click on the Shipping, select Schedule a Pickup, and look on the right side of screen to click on "Pickup Request Status". Enter in the Pickup No. listed on receipt into PRN field and submit

Airbill





Accessing Airbill

- Print out the UPS air waybill
- Fold the UPS air waybill and slide it inside the plastic UPS sleeve (NCRAD will provide these in kit requests)
- Peel the back off the plastic UPS sleeve and stick the sleeve to your package, making sure it is laying as flat as possible along the surface of the package.

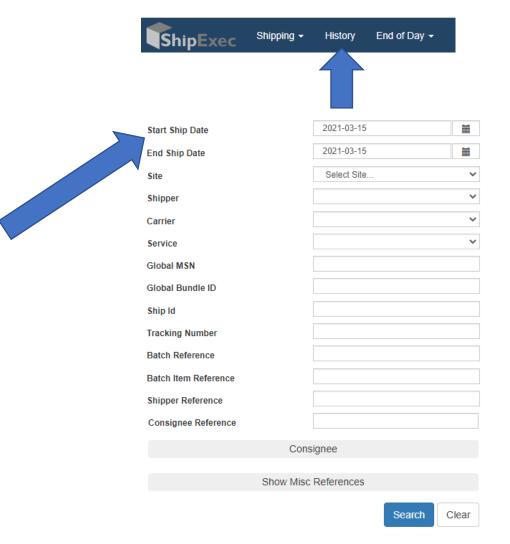




Reprint Airbills/Voiding Shipments

 To reprint airbill or void a shipment, click "History" at the top of the ShipExec Thin Client portal

• If your shipment doesn't automatically pop up, enter in the date of shipment and then click "Search"





Reprint Airbill

Click the print icon to reprint airbill

Action	Global MSN	Tracking Number \$	Shipper Reference	Consignee Reference	Ship Date ^{\$}	Weight	Rated Weight [‡]	Dimension
Q 😛 🚊	9506	1Z976R8W8430841976		6683830	2020- 12-08	20 LB	20 LB	



Void Shipment

To void a shipment, click on the "X" symbol

Action	Global MSN	Tracking Number 	Shipper Reference	Consignee Reference	Ship Date ^{\$}	Weight	Rated Weight [‡]	Dimension
Q 🙃 🚊	9506	1Z976R8W8430841976		6683830	2020- 12-08	20 LB	20 LB	



Creating a ShipExec Account

- Please email the NCRAD Coordinator if you do not have a ShipExec Account:
 - Zoë Potter <u>zdpotter@iu.edu</u>
- Once your ShipExec account is created, you will get an email from noreply@shipexec.com. This email will have a temporary password in the body of the email. Login using this password.
- You will then be prompted to reset your password.
- Look in your junk folder in case the email is being incorrectly flagged.



Blood Sample and Shipment Notification Form





A copy of the sample form *must* be emailed to NCRAD prior to the date of sample arrival.

Blood Sample and Shipment Notification Form



Please include sample forms in all shipments of frozen samples.



Email: alzstudy@iu.edu



Appendix B: Biological Sample and Shipment Notification Form





				A	ppendix B: I	Biological	l Sample and S	hipment	Noti	fication Form		Con	sortium
			To	: Kelley Fa				Phone: 1-					
IPS track	ing #:	1 Z 97	76R8V	٧				Date:_					
rom:					Pho	ne:			E	mail:			
									<u></u>				
Study: CA	ADASI	L Sit	te ID:_		CADASIL INC	#: <u>CC</u>				107			
Sex: M	l F	Ye	ar of E	Birth:						KILE	BARCODE		
Visit:	Baselir	ne	18 M	Month	36 Month				Ĺ				زــــا
Blood Co	llectio	n:											
			Date	of Draw:			[MMDDYY]	Time of	Draw	r:	[HHMM]		
			Date:	subject las	t ate:		[MMDDYY]	Time su	bject	last ate:	[HHMM]		
Γ						RI	NA (PAXgene™ 1	Tubes)					
Ţ	#1			Number				T					
	+			ı r digits) : Number		Origina	il volume drawn	:	_ml	Time PAXgene™			
1	#2			r digits):		Origina	al volume drawn	:	_ml	tubes placed in freezer:		[HHMM]	
Blood Pro	ocessir	ıg:											
						Serur	n (Red-top) Tub	e (8.5 mL)				
Ti	ime sp	in sta	rted:		_[HHMM]		Number of 0).25 mL se	rum a	aliquots created (re	d cap):		
Durati	on of	centri	ifuge:		Mins		Number of	1.5 mL se	rum a	aliquots created (re	ed cap):		
Ten	np of (Centri	ifuge:		°C	of residual seru	um aliquot (less than 1.5 mL in blue cap):				m	L N/A	
Ra	ate of	centri	ifuge:		x g Specimen num			number of residual serum aliquot (last four digits):					N/A
Origina	al volu	me di	rawn:		_mL			Time aliquots placed in freezer:					нмм]
	Time	aliqu	oted:		[HHMM]			9	Storag	reezer:	°C	;	
					Plasn	na & Buffy	Coat (Lavender						
		Tin	ne spin	started:		[HHMM]				Time aliq	uoted:	[H	ними]
	_		_			Nu	Number of 0.25 mL plasma aliquots created						
	Du	ratio	n of ce	ntrifuge:		Ains	(purple cap): Number of 1.5 mL plasma aliquots created						
		Tem	p of Ce	ntrifuge:		С	(purple cap):						
		D-4			_	_	Volume of residual plasma aliquot					1	
		Kdl	e or ce	ntrifuge:		g	(less than 1.5 mL in blue cap): Specimen number of residual plasma aliquot					m	L N/A
Original volume drawn - EDTA #1			EDTA #1	mL		(last four digits):						N/A	
Original volume drawn - EDTA #2			mL		Time aliquots placed in freezer:					[H	нмм]		
Original volume drawn - EDTA #3			mL		Storage temperature in freezer:					°C			
Original volume drawn - EDTA #4			mL										
Aliquot volume – Buffy coat #1			r	nL	Buffy coat aliquot #1 (last four digits):								
Aliquot volume – Buffy coat #2			r	nL	Buffy coat aliquot #2 (last four digits):								
Aliqu	uot vo	lume	– Buff	y coat #3	mL			Buffy coat aliquot #3 (last four digits):					
Aliqu	uot vo	lume	– Buff	y coat #4	r	nL		Buffy c	oat a	liquot #4 (last four	digits):		
NOTES:													



It is critical that the tube be centrifuged at the appropriate speed to ensure proper serum and plasma separation. Use Rate of Centrifugation Worksheet to calculate RPM.

Appendix A: Rate of Centrifugation Worksheet

Please complete and return this form by email to the NCRAD Project Manager if you have any questions regarding sample processing. The correct RPM will be sent back to you.

Submitter Information

Name: Site Submitter e-mail:

Centrifuge Information

Please answer the following questions about your centrifuge.

Centrifuge Type

Fixed Angle Rotor: ☐ Swing Bucket Rotor: ☐

Radius of Rotation (mm):

Determine the centrifuge's radius of rotation (in mm) by measuring distance from the center of the centrifuge spindle to the bottom of the device when inserted into the rotor (if measuring a swing bucket rotor, measure to the middle of the bucket).

Calculating RPM from G-Force:

$$RCF = \left(\frac{RPM}{1,000}\right)^2 \times r \times 1.118 \quad \Rightarrow \quad RPM = \sqrt{\frac{RCF}{r \times 1.118}} \times 1,000$$

RCF = Relative Centrifugal Force (G-Force)

RPM = Rotational Speed (revolutions per minute)

R= Centrifugal radius in mm = distance from the center of the turning axis to the bottom of centrifuge

Comments:

Please send this form to NCRAD Study Coordinator at alzstudy@iu.edu

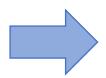


Noncomformance Issues



Nonconformance Issues

Sample aliquots and collection tubes frozen at an angle/inverted



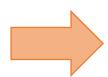
Recommendation:

Place aliquots in cryoboxes/tube rack in freezer *upright* until shipment

Fields left blank on Blood Sample and Shipment Notification Form

Last time subject ate often left blank/unknown

Incorrect data reported on Sample and Shipment Notification Forms



Recommendation: Complete Sample Notification forms during the participant study visit as samples are processed.

Nonconformance Issues

All frozen samples for a participant not sent within one shipment box (plasma and buffy coat aliquots should be kept together)

Aliquots arriving to NCRAD without labels

Sample forms not scanned to NCRAD the day before shipment

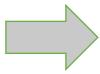


Recommendation:

Ship Samples to NCRAD utilizing the Notification Form, by PTID. Do not throw away labels until samples are packed and shipped.

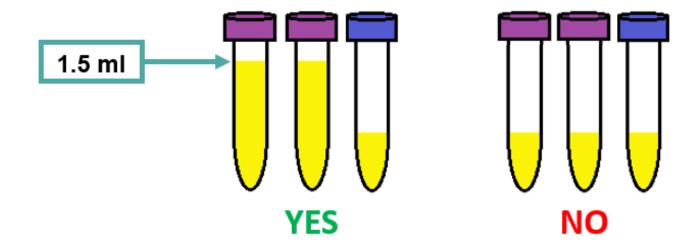
Nonconformance Issues

Multiple low volume aliquots



Recommendation:

Lay out cryovials in a row and aliquot in order until sample is depleted



NCRAD Website



NCRAD Website: Helpful Pages

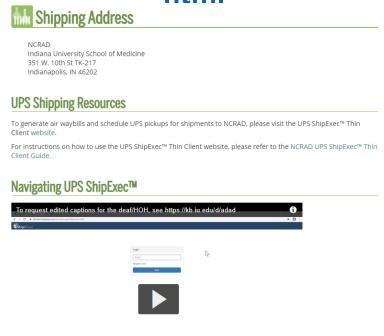
NCRAD - CADASIL Active Study Page

https://ncrad.org/holiday_closures.h tml



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				

https://ncrad.org/shipping_address.html





Contact Information

Questions?

Zoë Potter, Study Coordinator

Phone: (317) 278-9086

Email: zdpotter@iu.edu

General NCRAD Contact Information

Phone: 1-800-526-2839

Email: alzstudy@iu.edu

