Clinical Trials Central Laboratory Manual

Protocol: Efficacy of Isradipine in early Parkinson Disease

Study Identifier: STEADY – PD III

URMC Study Identifier: U080800015

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Section 1. Laboratory Contacts

Our staff is available to assist the Investigative Sites with requests for supplies, lab reports, changes in demographic and collection information, specimen collection, packaging, and shipping instructions.

To contact the University of Rochester / ***URMC Labs*** Clinical Trials Central Laboratory, please utilize the following information:

Mailing Address:	URMC Labs - CTCL 77 Ridgeland Road Room 139- Specimen Logistics Rochester, NY 14623
Toll Free #:	800-405-1889
Local Phone #:	585-758-0525
After hours Cell Phone #:	585-690-5310
After hour's pager #:	585-220-0757
Study Support Fax #:	585-419-6115
Shipment Notifications Fax #:	585-486-1589
Study Supplies Order Fax #:	585-486-1375
Study Support e-mail address:	LabSRSS@urmc.rochester.edu
Project Management Hours:	Mon – Fri, 8:00 AM – 6:00 PM EST
Project Manager:	Panos Ginis
Telephone Number:	800-405-1889 or 585-758-0445 (direct)
Email Address:	Panos_Ginis@URMC.rochester.edu
Dry Ice Directory:	http://www.dryicedirectory.com/usa.htm

Section 2. Laboratory Hours of Operation

URMC Labs operate 24 hours a day / 365 days per year.

Clinical Trials testing is performed Monday – Saturday, unless other arrangements have been made for a specialized courier service to deliver specimens on Sundays for testing.

Federal Express does not offer Sunday delivery service to URMC Labs.

Holiday Schedules

Based on previous years, FedEx observe the holidays listed on the next page. These dates are subject to change by FedEx.

Should we receive adequate advance notice of a change in schedule, we will provide an updated schedule to your site. However, it is ***strongly recommended*** that you verify your FedEx's schedule prior to any holiday.

- Avoid collecting specimens for shipment on the day before an observed holiday.
    - If a patient's visit falls on the day before a scheduled holiday, please contact URMC Labs to determine how to best handle the specimen shipment.

Section 2. Laboratory Hours of Operation (Continued)

Holiday Observations

2014 Dates	Holiday
Thursday, November 27	Thanksgiving
Thursday, December 25	Christmas
2015 Dates	**Holiday**
Thursday, January 1	New Year's Day
Monday, May 25	Memorial Day
Saturday, July 4	Independence Day
Monday, September 7	Labor Day
Thursday, November 26	Thanksgiving
Friday, December 25	Christmas
2016 Dates	**Holiday**
Friday, January 1	New Year's Day
Monday, May 30	Memorial Day
Monday, July 4	Independence Day
Monday, September 5	Labor Day
Thursday, November 24	Thanksgiving
Sunday, December 25	Christmas
2017 Dates	**Holiday**
Thursday, January 1	New Year's Day
Monday, May 29	Memorial Day
Tuesday, July 4	Independence Day
Monday, September 4	Labor Day
Thursday, November 23	Thanksgiving
Monday, December 25	Christmas
2018 Dates	**Holiday**
Monday, January 1	New Year's Day
Monday, May 28	Memorial Day
Wednesday, July 4	Independence Day
Monday, September 3	Labor Day
Thursday, November 22	Thanksgiving
Tuesday, December 25	Christmas

Note: URMC Labs will provide e-mail notification of FedEx holiday schedules as it becomes available.

Section 3. Protocol Laboratory Testing Schedule

Patients will have central laboratory testing according to the following schedule.

Visit and Test Schedule:

Test	Screen[1]	V03	V04	V06	V08	V10	PW	UNS[2]	STX[4]
Chemistry	X			X	X	X	X	X	X
Hematology	X			X	X	X	X	X	X
Urinalysis	X			X	X	X	X	X	X
Serum Pregnancy Test[3]	X			X	X	X	X	X	X
PK Samples[5]	X	X	X				X[6]		
Plasma Biomarkers[7]	X					X	X		
DNA Sample Collection[7]	X								

[1]Rescreening visits will be allowed
[2]If an Unscheduled visit is scheduled to reduce antihypertensive medication, the visit will include all V01 laboratory testing. Otherwise, laboratory testing will be collected as clinically indicated.
[3]Complete serum pregnancy test for all women unless they are one year postmenopausal or surgically sterile.
[4]If the symptomatic treatment visit occurs within the window of a regularly scheduled study visit, the symptomatic treatment visit will be completed in place of the regularly scheduled study visit. If this visit is conducted in place of the regularly schedule V06, V08 and V10, visit assessments will include the following additional assessments: safety labs and pregnancy test[2].
[5]A PK sample will be collected at Screen. A pre and post PK sample will be collected at V03. A post PK sample will be collected at V04.
[6]PK will be collected at Premature Withdrawal visits when it coincides with the timeframe of V03 or V04.
[7]DNA and Biomarker sample collection is optional for subjects who consent to provide a DNA or biomarker sample for storage and future, unspecified research.

Section 4. Specimen Collection Kits

URMC Labs will provide all materials for the collection and shipment of specimens used for central laboratory testing.

URMC Labs DOES NOT provide dry ice for frozen shipments. Please go to http://www.dryicedirectory.com/usa.htm for a directory of dry ice providers.

Should you have any questions about specimen collection, processing, storage, packaging or shipping, please contact URMC Labs at 800-405-1889.

Additional supplies may be requested by faxing a completed URMC Labs Kit Re-Supply Form to 585-486-1375 or email to LabSRSS@urmc.rochester.edu. Kit Re-Supply forms are included in the pocket of this lab manual. Please allow 7 to10 business days for supplies to reach your site. If your request is urgent, please note that on your form.

Kits Supplied at Initiation:

Kit Name	# Kits Shipped at Initiation
Screening (may be used for rescreening, as needed)	4
PK visit 1*	4
PK visit 2*	2
Multi visit 1	2
Multi visit 2	1

**Insulated shippers will be provided for frozen specimens to be shipped to the central lab every 6 months.

Section 4. Specimen Collection Kits (Continued)

Kit Name	Kit Contents	# Kits Supplied at Initiation
Screening	1 – 5 mL Gold SST tube 1 – 4mL yellow capped cryovial 1 – 4 mL Lavender top EDTA tube 1 – 3 mL Na Heparin tube 2 – 1.5mL cryovials 1 – 6 mL Lavender top EDTA tube 4 –1.5 mL purple capped cryovials 2 – 8.5mL Yellow ACD top EDTA tube 1 – Urine Collection Kit 1 – Blood Collection Kit 1 – Hematology Slide Kit 4 – Transfer Pipettes 1 – Test Requisition 1 – Set of uniquely numbered Kit ID Labels 2 – 95 kPa bags	4
PK visit 1 Kit[1]	2 – 3 mL Na Heparin tubes 4 – 1.5 mL cryovials 2 – Blood Collection Kits 2 – Transfer Pipette 2 – Test Requisitions 2 – Sets of uniquely numbered Kit ID Labels 1 – 95 kPa bag	4
PK visit 2 Kit[2]	1 – 3 mL NA Heparin tubes 2 – 1.5 mL cryovials 1 – Blood Collection Kit 1 – Transfer Pipette 1 – Test Requisition 1 – Set of uniquely numbered Kit ID Labels 1 – 95 kPa bag	2
Multi Visit 1[3]	1 – 5 mL Gold SST tube 1 - 4mL yellow capped cryovial 1 – 4 mL Lavender top EDTA tube 1 – Urine Collection Kit 1 – Hematology Slide Kit 1 – Transfer Pipette 1 – Test Requisition 1 – Set of uniquely numbered Kit ID Labels 1 – 95 kPa bag	2
Multi Visit 2[4]	1 – 5 mL Gold SST tube 1 - 4mL yellow capped cryovial 1 – 4 mL Lavender top EDTA tube 1 – 6 mL Lavender top EDTA tube 4 –1.5 mL purple capped cryovials 1 – Urine Collection Kit 1 – Blood Collection Kit 1 – Hematology Slide Kit 2 – Transfer Pipettes 1 – Test Requisition 1 – Set of uniquely numbered Kit ID Labels 2 – kPa bags	1

1 For V03/ Month 3 and PW visits where the PW visit coincides with V03
2 For V04/ Month 4 and PW visits where the PW visit coincides with V04
3 For V06, V08, UNS, STX visits
4 For V10 visit and PW when the PW visit does not coincide with V03 or V04 visits

Section 4. Specimen Collection Kits (Continued)

Additional Supplies

- Investigator Manual
- Extra collection tubes and requisitions

Shipping Containers Provided at Initiation

- Ambient shippers including silver pouch, gel packs and FedEx waybills
- For sites with access to long term freezer storage:
  - 4 Ambient Shippers including silver pouch, gel packs and FedEx waybills.
-
- Shipping materials will be provided to you for bi-annual shipments of frozen specimens. These materials will include a cooler of an adequate size to accommodate the shipment of specimens in storage at your site.

Section 4. Specimen Collection Kits (Continued)

Useful Documents Supplied at Initiation in Folder Packet:

- Kit Re-Supply Form
- Shipment Notification Form
- Data Correction Request Form
- Site Information Change Form
- Extra Test Requisitions
- Dry Ice Labels

Kit Re-Supply Process

- Sites will monitor inventory and order kits supplies as indicated by enrollment and study schedule.
- URMC Labs will monitor kit expiration and notify site should their kit inventory be subject to expiration within the next 4 weeks.
- Additional supplies may be requested by faxing a completed URMC Labs Kit Re-Supply form to 585-486-1375 or emailing a completed URMC Labs Kit Re-supply form to LabSRSS@urmc.rochester.edu. The URMC Labs Kit Re-supply form is included in the pocket of this lab manual.
- All supplies will be dispatched from URMC Labs within 5 to 7 business days of receipt of a request. Supplies will be delivered to the sites via ground courier service, so please allow 7 to 10 business days for supplies to reach your site. Additional costs may be incurred should a faster delivery time be required.

Outbound Shipping

- Specimens will be shipped Priority Overnight from the investigator site to URMC Labs Monday through Friday. Packages shipped Friday **MUST** be marked for Saturday delivery.
- Frozen specimens should be shipped Priority Overnight from the investigator site to URMC Labs Monday through Wednesday **ONLY** so please plan accordingly.
- Specimens will be shipped via FedEx with charges billed to URMC Labs Reference #: STEADY – PD III, site no. ###

Section 5. Test Requisitions

Test requisitions have been specifically designed to accurately capture the data elements required for the protocol. Failure to properly complete the test requisition will result in issuance of a data query and may delay the receipt of the results reported to your site.

Each kit will be provided with a set of uniquely numbered specimen Kit ID labels. A Kit ID footie label is included to be affixed to the test requisition (see Test Requisition section of the lab manual for placement of Kit ID footie label on test requisition).

Required Elements on requisition

- Required Patient Identifiers
    - Site Number (3 digit, example, '123')
    - Subject ID (4 digit, example: '0010')
    - Subject Date of Birth: DD/MMM/YYYY
    - Gender: M/F
- Specimen Collection Date: DD/MMM/YYYY
- Specimen Collection Time: HH:MM (24 hour clock)
- Visit
- Signature of person who collects the sample

Documentation Guidelines

The information captured on the test requisition must match the Case Report Form.

In the event that information documented on the test requisition needs to be corrected, place a single line through the incorrect information, clearly write the corrected information, and date and initial the change in accordance with GCP requirements.

Make sure to keep the yellow copies of the test requisitions for your records!

Canceled Testing / Additional Test Requests

Should a test need to be canceled or a specimen cannot be collected, note the word "Canceled" next to the test / specimen name. Use the comments section at the bottom of the form to provide any additional information regarding the canceled test (Example: 'Subject unable to void').

Requests for testing that is not part of the protocol will not be allowed for the STEADY – PD III study.

Section 5. Test Requisitions (Continued)

Test Requisition Completion and Kit ID label Placement:

1) Record subject ID, gender, DOB and collection date and time on test requisition, as shown:

2) Record Name of person collecting samples under 'Collected By:'

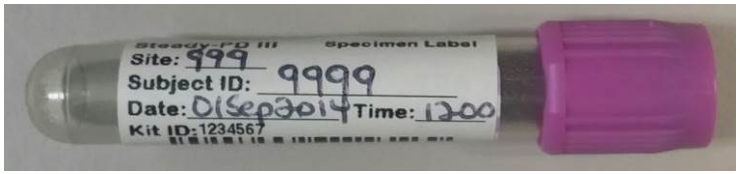
3) Select the Subject's visit on the following requisitions.

Kit ID footie label

Place small Kit ID footie label on the test requisition

Draw / aliquot tube Kit ID label:

Fill in Subject ID, collection date and time, and place the completed Kit ID label horizontally on the draw tubes and any aliquot tubes as shown:



URMC LABS

Apply "Requisition Label" from Kit Label Strip:

Ordering Physician: Sample Investigator
Coordinator: Test Coordinator
Phone: **Fax:**

Protocol: STEADY PD III **ClinAxys: U080800015**

3

☒ Screening ☐ Rescreening

Site Number:	Subject ID:	Gender:	Date of Birth: DD	MMM	YYYY
999	9999	F	01	JAN	1980

1

Collection Date & Time: DD: 01 MMM: SEP YYYY: 2014 HH: 12 MM: 00 (24 Hour Clock)

☒ Biomarker collection is optional. Check box if sample is collected.

☒ DNA collection is optional. Check box if sample is collected.

☒ Check box if FEMALE subject is of Child Bearing potential. If 'YES' the SPREG testing will be added. SPREG will NOT be automatically performed on female subjects.

2

Collected By: Study Coordinator (Insert Collector's Name)

TEST NAME		SHIPPING	URMC LAB USE
Chem Panel SPREG	Collect one 5mL gold top serum separator tube; gently invert each tube 8-10 times. Allow blood to clot upright at room temperature for 30 minutes. Centrifuge for 10 minutes at 1500 x g. Aliquot serum into 4mL yellow top cryovial.	AMBIENT	____ 4mL Yellow Cryovial
CBCD	Collect one 4mL Lavender top tube; gently invert tube 8-10 times. Make two blood smears per instructions in lab manual. Do Not Centrifuge. Do Not aliquot.	AMBIENT	____ 4mL Lav ____ Slides
Urinalysis	Connect yellow and red marble capped urine tube to the integrated device in the cup lid to transfer urine from the random void, gently invert 8-10 times.	AMBIENT	____ UA Marble Tube Top
PK	Collect one 3mL green top tube; gently invert tubes 8-10 times. Centrifuge for 10 minutes at 1500 x g. Aliquot plasma into (2) clear top cryovials. Immediately freeze at site at -80°C.	FROZEN	____ 1.5mL cryovials
Optional samples:			
DNA	Collect two 8.5mL yellow ACD tubes; gently invert tubes 8-10 times. Do not Centrifuge; Do Not aliquot.	AMBIENT	____ 8.5mL Yellow ACD tubes
Biomarkers	Collect one 6mL Lav top tube; gently invert tube 8-10 times. Centrifuge for 10 minutes at 1500 x g. Aliquot plasma into (4) 1.5 mL lavender capped cryovials. Immediately freeze at -80°C.	FROZEN	____ 1.5mL lav cryovials

COMMENTS AND ADDITIONAL INFORMATION

Tech initials: _____

Date _____

LAB USE ONLY Shipping Supplies: _____ kPa Bag _____ Gel Packs _____ Pillow
Version: 09Sep2014
White Copy - Send to Lab with Ambient Specimens Yellow Copy - Retain in Study File at Site Pink Copy – Keep with Frozen Samples

Section 6 Specimen Collection and Preparation

<table>
<tr><th colspan="3">Safety Labs</th></tr>
<tr>
<td>  </td>
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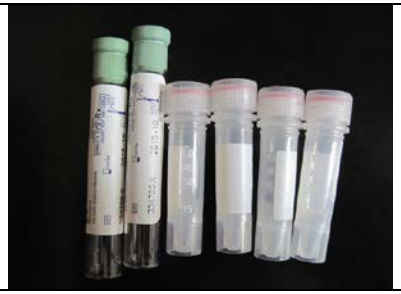
<tr>
<td>Chemistry Panel/ Serum Pregnancy
➢ Completely fill a 5 mL Gold top Serum Separator Tube (SST) with blood
➢ Gently invert tube 8 to 10 times
➢ Allow blood to clot for 30 minutes
➢ Centrifuge SST at 1500 x g for 10 minutes
➢ Transfer serum into the 4mL yellow topped aliquot tube
Send aliquot to URMC Labs</td>
<td>CBC/ Diff
➢ Completely fill a 4 mL Lavender top EDTA Tube with blood
➢ Gently invert tube 8 to 10 times
➢ Make blood smear (see diagram)
➢ DO NOT CENTRIFUGE
➢ DO NOT ALIQUOT
Send both Lavender tube <u>and</u> slides to URMC Labs</td>
<td>Urinalysis
➢ Collect urine in specimen collection cup
➢ Connect yellow and red marble top urine tube to the integrated device in the cup lid to transfer urine from the random void
➢ Discard collection cup and any remaining urine
Send urine tube to URMC Labs. fa</td>
</tr>
<tr>
<td>Ship:
➢ Ambient
➢ Priority Overnight
➢ To URMC Labs</td>
<td>Ship:
➢ Ambient
➢ Priority Overnight
➢ To URMC Labs</td>
<td>Ship:
➢ Ambient
➢ Priority Overnight
➢ To URMC Labs</td>
</tr>
</table>

Section 6 Specimen Collection and Preparation (Continued).

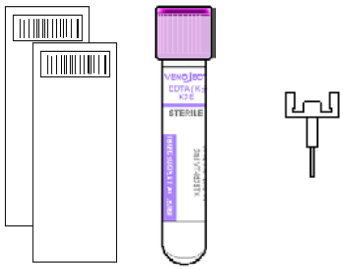
PK, Biomarker, DNA			
PK – Screen, V04	PK – V03	Biomarker	DNA
			
➢Completely fill a 3 mL Green top tube with blood ➢Gently invert tube 8 to 10 times. ➢Centrifuge Green top at 1500 x g for 10 minutes ➢Transfer plasma into the (2) 1.5 mL green capped cryovials ➢Immediately freeze cryovials at -80°C *Freeze at site until batch shipment to URMC Labs*	➢At predose and post dose visit, fill a 3 mL Green top tube with blood. ➢Gently invert tube 8 to 10 times. ➢Centrifuge Green top at 1500 x g for 10 minutes ➢Transfer plasma into 1.5 mL cryovial labeled predose or postdose. ➢Immediately freeze cryovials at -80°C *Freeze at site until batch shipment to URMC Labs*	➢Completely fill a 6 mL Lav top tubes with blood ➢Gently invert tube 8 to 10 times. ➢Centrifuge Lav top at 1500 x g for 10 minutes ➢Transfer plasma equally into (4) 1.5 purple capped cryovials ➢Immediately freeze cryovials at -80°C *Freeze at site until batch shipment to URMC Labs*	➢Completely fill (2) 8.5 mL Yellow ACD tubes with blood ➢Gently invert tube 8 to 10 times. ➢DO NOT CENTRIFUGE ➢DO NOT ALIQUOT *Send to URMC Labs*
Ship: ➢ Batch ship frozen* ➢ Priority Overnight to URMC Labs M-W *ONLY*	Ship: ➢ Batch ship frozen* ➢ Priority Overnight to URMC Labs M-W *ONLY*	Ship: ➢ Batch ship frozen ➢ Priority Overnight to URMC Labs M-W *ONLY*	Ship: ➢ Ambient ➢ Priority Overnight ➢ To URMC Labs

* One of the two aliquouts will be considered “primary” and the other “secondary”. Primary and secondary aliquots from a single lab visit will be shipped at separate times.

Preparation of blood smears

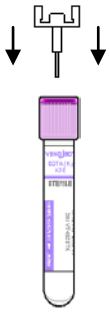
Label all tubes and slides with the required information. Be sure the labels correspond with appropriate clinical trials requisition.

1



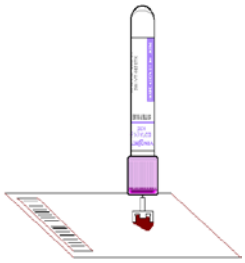
Blood slides must be prepared from the EDTA (lavender) sample. **Label frosted end of both slides in pencil with subject ID number.**

2



Gently invert the EDTA tube 8-10 times. Following specimen collection insert the blood dispenser device through the stopper of the tube held in the upright position.

3

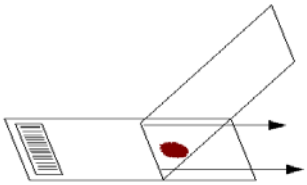


Place slide on flat surface. Turn the tube upside down and press moderately against slide. Place a small drop of blood near one end of the pre-labeled slide.

4

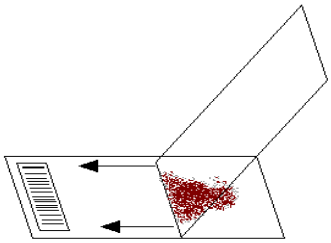
With slide remaining on flat surface, hold one edge (furthest away from blood) of the slide.

5



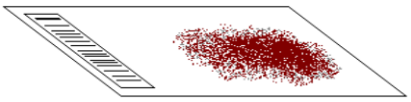
Place the edge of the second slide at a 30° angle in front of the droplet of blood. Move slide backwards until it makes contact with the blood. Pause to allow the blood to spread along the edge of the slide.

6



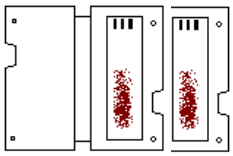
With a quick, smooth motion, push the slide forward, dragging the blood toward the opposite edge to make the smear. As you push, the blood film should become thinner leaving a final feathered edge.

7

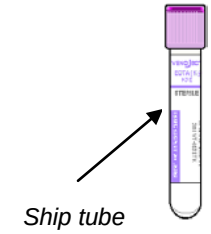


Let slide dry then repeat steps 4-6 for the second slide. When both slides are dry, place them in the slide holder.

8



9



Ship tube and slides ambient to URMC Labs

Requires Biohazard Sharp Disposable

Section 7. URMC Labs Sample Shipment

Once samples are processed and ready to send, fax the 'Shipment Notification' form to 585-486-1589 or email it to LabSRSS@urmc.rochester.edu.

If you have any questions or concerns, please call the Clinical Trials department at 585-350-2670. Or call Panos Ginis, 585-758-0445 (direct phone line).

Section 7. Ambient Packaging and Shipping Instructions

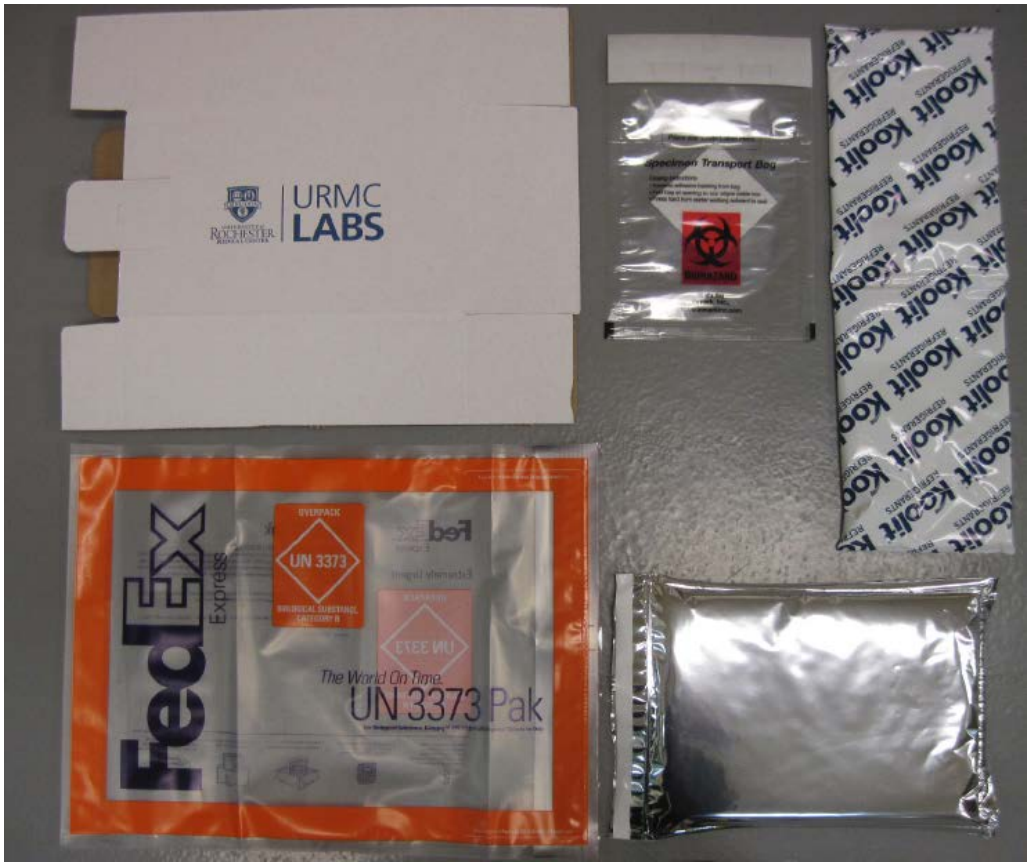
Sample Shipments

The URMC packaging and labeling provided is designed to:

- Maintain the viability of the specimen(s) during shipping
- Protect the specimen(s) from damage during shipping
- Ensure the proper routing and handling of packages when received at our facility
- Comply with IATA (International Association of Air Transportation) and US D.O.T. (Department of Transportation) regulations
- All samples must be shipped in IATA compliant Specimen Transport Bags (95 kPa Bags).

Use of materials other than described above may compromise the sample.

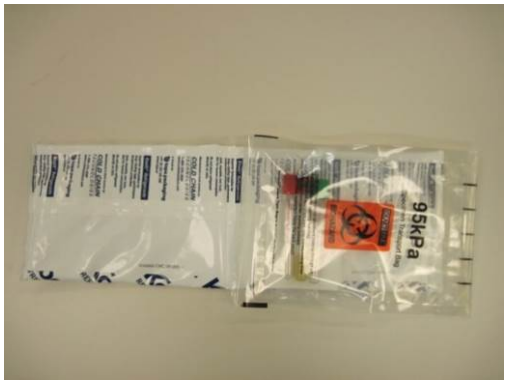
Ambient Shipping System Supplies



Section 7. Ambient Packaging and Shipping Instructions (Continued)

Step 1 – Place Tubes in 95 kPa bag and Seal

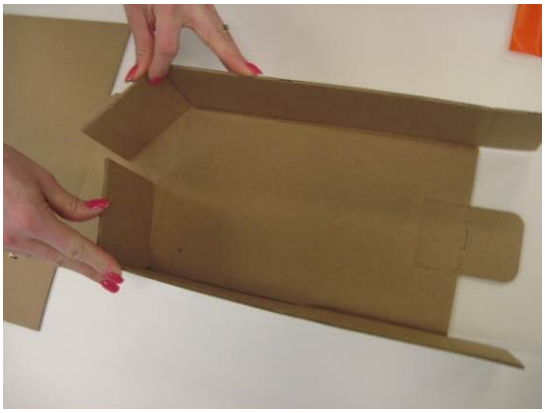
Step 2 – Place sealed 95 kPa bag on top of one half of Gel Pack and then fold Gel Pack over the top of the sealed kPa bag

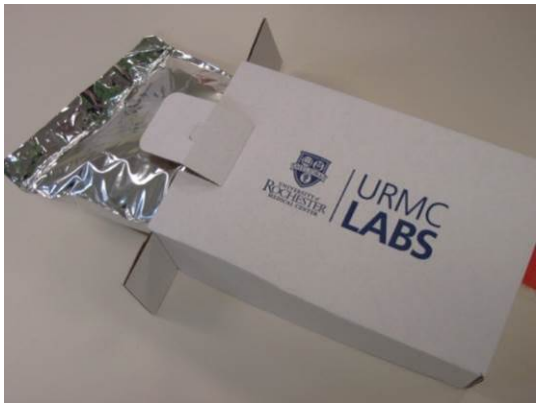


Step 3 – Place Gel Pack and 95 kPa bag inside insulated silver pouch and use zip lock to seal

Section 7. Ambient Packaging and Shipping Instructions (Continued)

Step 4 – Fold ambient shipper to create a box and place insulated silver pouch inside. Use tab to secure box. No additional tape or sealant is required!





Section 7. Ambient Packaging and Shipping Instructions (Continued)

Step 5 – Place box inside FedEx Clinical Pak and seal using the self-adhesive tape strip

Step 6 – Complete the FedEx Waybill and attach to the outside of the Clinical Pak

Section 7. Ambient Packaging and Shipping Instructions (Continued)

Ship the ambient samples immediately following collection of the sample Monday - Friday via FedEx overnight priority express courier to:

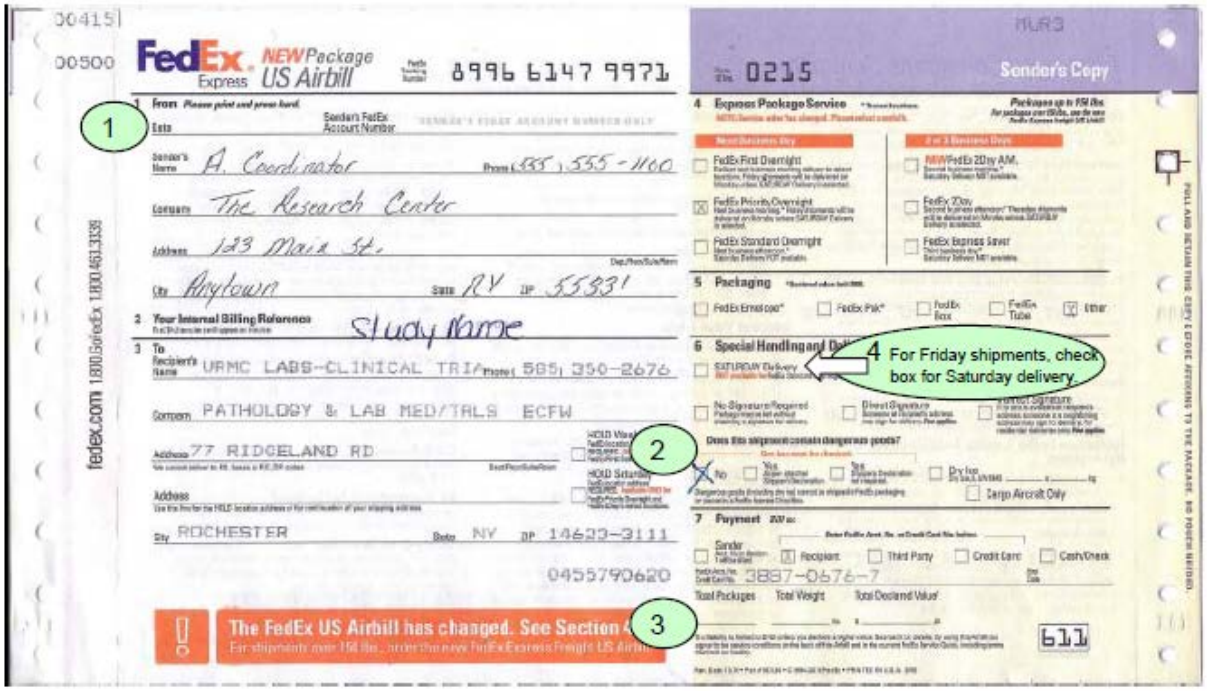
URMC Labs
77 Ridgeland Road
Rochester, NY 14623

Packages shipped on a Friday must be marked for Saturday Delivery.

Notification of Shipment: Complete the **Shipment Notification Form** (included in the pocket of this lab manual) and email a copy to URMC Labs Study Support at LabSRSS@urmc.rochester.edu or fax it to 585-486-1589.

Call FedEx at 1-800-463-3339 to schedule a pick up.

AMBIENT SHIPPING INSTRUCTIONS



1. Using the pre-printed air bills supplied, enter the shipment **date** in Section 1.
2. Check **"NO"** Under Section 6- Special Handling and Delivery, **Does this shipment contain dangerous goods?**
3. Enter the **Total Weight** of the package in lbs.
4. For **Friday shipments**, **Check** the box for **Saturday Delivery!**

Section 8. Frozen Shipping Instructions and Schedule

Sample Shipments

Sites will ship frozen samples to URMC Labs every 6 months.
A general schedule of months that each site will ship will be provided to the Clinical Trials Coordination Center and posted to the eClinical study portal."
URMC Labs will provide each site with notification of when to ship frozen samples and will provide a cooler of an adequate size to accommodate the frozen specimens in storage at the site.

Frozen samples for PK testing will be divided into primary and secondary aliquots. **Primary aliquots** will be shipped in one scheduled shipment and the **secondary aliquot** will be shipped with the following scheduled shipment.

Secondary PK aliquots should remain in storage at -70c or colder until shipment.

The URMC packaging and labeling provided is designed to:

- Maintain the viability of the specimen(s) during shipping
- Protect the specimen(s) from damage during shipping
- Ensure the proper routing and handling of packages when received at our facility
- Comply with IATA (International Association of Air Transportation) and US D.O.T. (Department of Transportation) regulations

All samples must be shipped in IATA compliant Specimen Transport Bags
(95 kPa Bags) with absorbent materials
Use of materials other than described above may compromise the sample.

Frozen Shipping System Supplies

Section 9. Frozen Packaging and Labeling Instructions (continued)

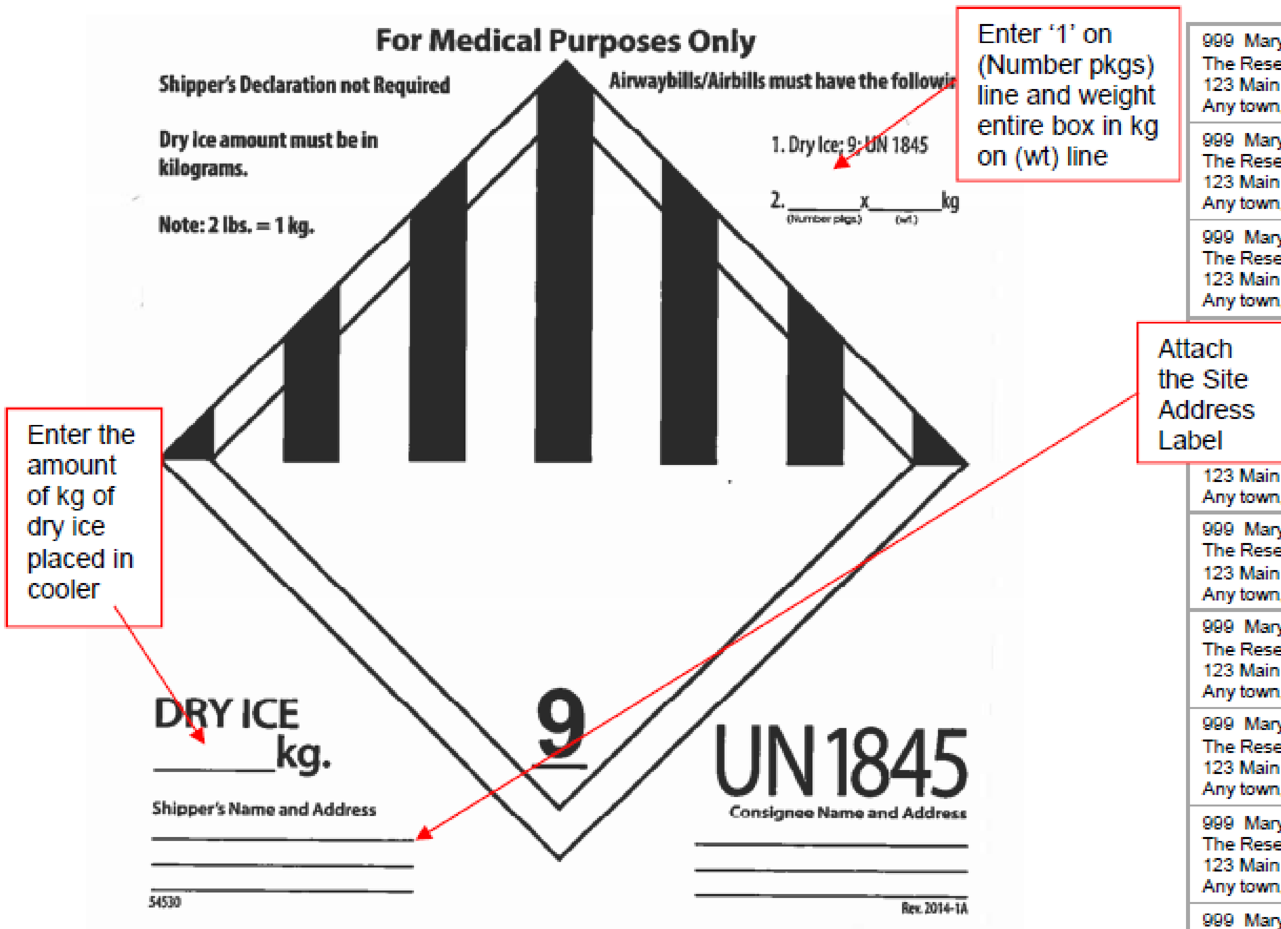
1. Place frozen specimens in 95 kPa bag and seal.

2. Place **at least 5 lb.** dry ice and packaged **Frozen** Specimens in inside the foam cooler section and place the lid on the cooler – Do Not Tape or Seal!

3. Close flaps and seal outer cardboard box.

Section 9. Frozen Packaging and Labeling Instructions (continued)

Complete dry ice information on box and attached FedEx air waybill for shipping



Site Address Labels

999 Mary Coordinator The Research Center 123 Main Street Any town, NY 55555	999 Mary Coordinator The Research Center 123 Main Street Any town, NY 55555	999 Mary Coordinator The Research Center 123 Main Street Any town, NY 55555
999 Mary Coordinator The Research Center 123 Main Street Any town, NY 55555	999 Mary Coordinator The Research Center 123 Main Street Any town, NY 55555	999 Mary Coordinator The Research Center 123 Main Street Any town, NY 55555
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Section 9. Frozen Packaging and Labeling Instructions (continued)

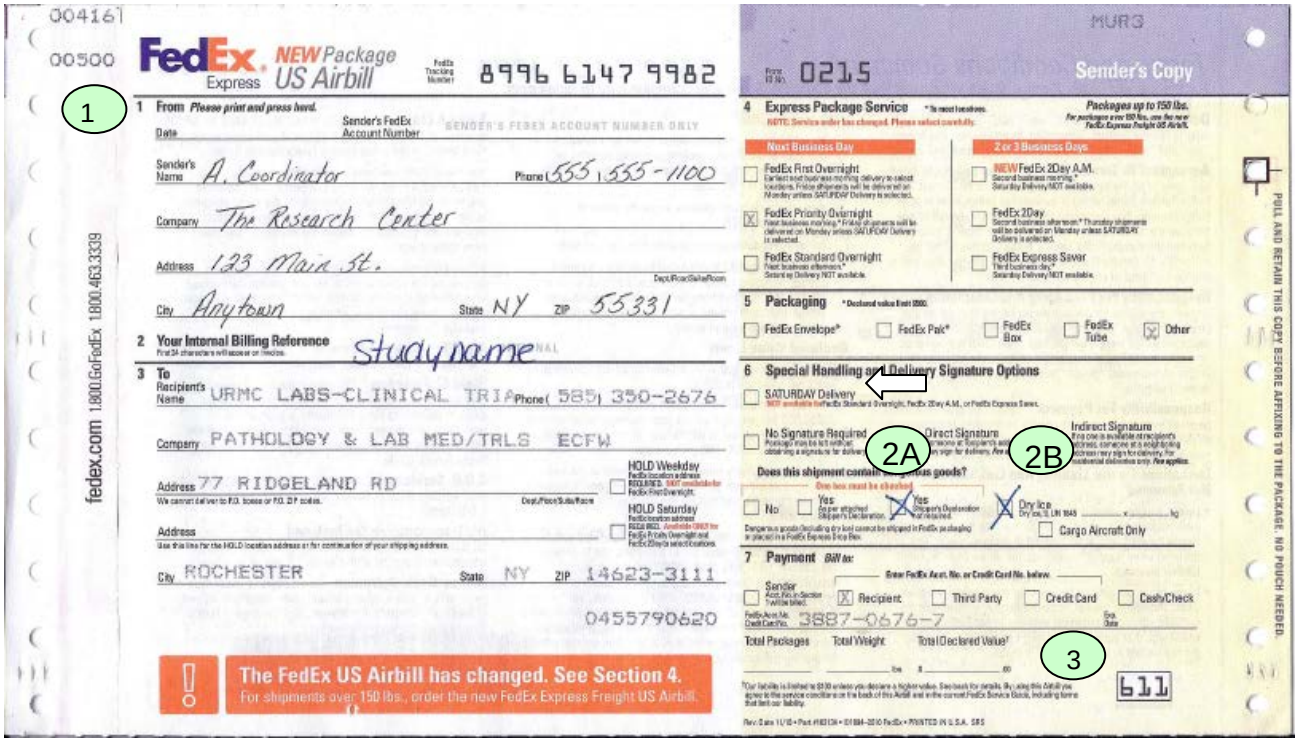
Ship the **Frozen** samples immediately following collection of the sample Monday – Wednesday via FedEx overnight priority express courier to:

URMC Labs
77 Ridgeland Road
Rochester, NY 14623

Notification of Shipment: Complete the **Shipment Notification Form** (included in the pocket of this lab manual) and email a copy to URMC Labs Study Support at LabSRSS@urmc.rochester.edu or fax it to 585-486-1589.

Call Fed Ex at 1-800-463-3339 to schedule a pick up.

FROZEN SHIPPING INSTRUCTIONS



1. Using the pre-printed air bills supplied, enter the shipment **date** in Section 1.
2. Under Section 6- Special Handling and Delivery:
   A. Check **"Yes- Shipper's Declaration not required"** under Section 6, **Does this shipment contain dangerous goods?**
   B. Check **"Dry Ice"** and enter the total weight of dry ice is kg (1 lb = 2.2 kg)
3. Enter the Total Weight of the package in lbs.

Frozen batch shipments of PK samples will only be shipped Monday through Wednesday.

Section 10. Laboratory Reports

Lab reports will be faxed to your office to the attention of the Coordinator / Investigator. A sample report is included in the appendices of this manual.

Report Turn Around Times

Testing will be completed and results reported within 24 hours of specimen receipt at URMC Labs.

Result Flags

Flag	Definition
*	Alert
H	High
VH	Very High
L	Low
VL	Very Low
Y	Yes
N	No

Results above the normal range for an assay will be flagged “H”.
Results below the normal range for an assay will be flagged “L”.

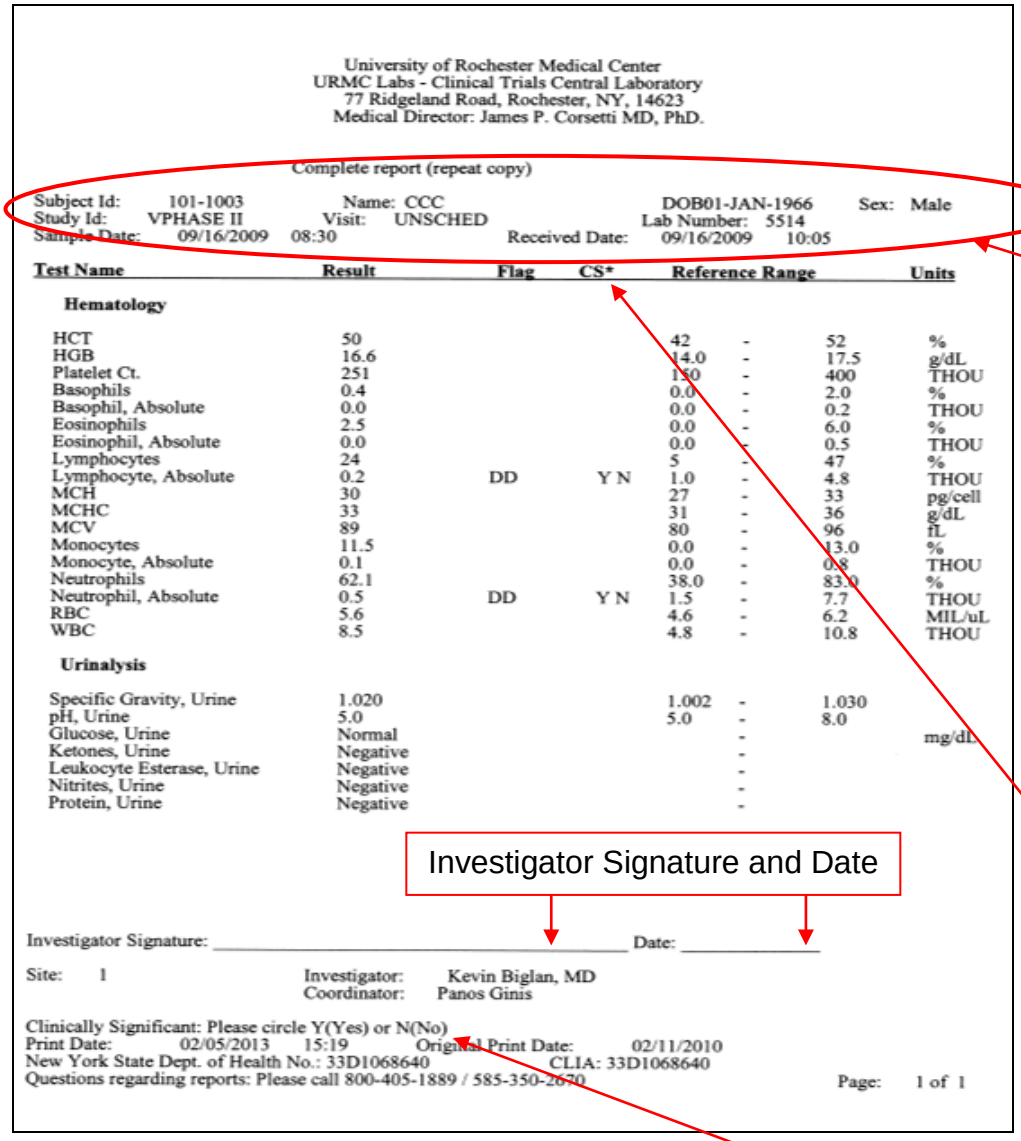
Results that are out of normal range may require additional follow up. The subject should be referred to his/her treating physician as necessary.

Alert Value Notification Specifications:

- Call Alerts, as defined below, will be promptly communicated via methods listed below in **Site Notification** section.

Analyte	URMC Labs Standard Alert Criteria		Site Notification
	Low	High	
Calcium	≤ 6.5	≥ 13.0	• Phone call and email report to medical monitor. • Phone call to investigator site during business hours and faxed report next business day.
Glucose	< 60	≥ 500	
Potassium	≤ 2.8	≥ 6.2	
Sodium	≤ 120	≥ 160	
WBC	< 3.0	≥ 50.0	
Hematocrit	≤ 19	female: > 45 Male: >51	

Section 10. Laboratory Reports



University of Rochester Medical Center
URMC Labs - Clinical Trials Central Laboratory
77 Ridgeland Road, Rochester, NY, 14623
Medical Director: James P. Corsetti MD, PhD.

Complete report (repeat copy)

Subject Id: 101-1003 Name: CCC DOB01-JAN-1966 Sex: Male
Study Id: VPHASE II Visit: UNSCHED Lab Number: 5514
Sample Date: 09/16/2009 08:30 Received Date: 09/16/2009 10:05

Test Name	Result	Flag	CS*	Reference Range	Units
Hematology					
HCT	50			42 - 52	%
HGB	16.6			14.0 - 17.5	g/dL
Platelet Ct.	251			150 - 400	THOU
Basophils	0.4			0.0 - 2.0	%
Basophil, Absolute	0.0			0.0 - 0.2	THOU
Eosinophils	2.5			0.0 - 6.0	%
Eosinophil, Absolute	0.0			0.0 - 0.5	THOU
Lymphocytes	24			5 - 47	%
Lymphocyte, Absolute	0.2	DD	Y N	1.0 - 4.8	THOU
MCH	30			27 - 33	pg/cell
MCHC	33			31 - 36	g/dL
MCV	89			80 - 96	fL
Monocytes	11.5			0.0 - 13.0	%
Monocyte, Absolute	0.1			0.0 - 0.8	THOU
Neutrophils	62.1			38.0 - 83.0	%
Neutrophil, Absolute	0.5	DD	Y N	1.5 - 7.7	THOU
RBC	5.6			4.6 - 6.2	MIL/uL
WBC	8.5			4.8 - 10.8	THOU
Urinalysis					
Specific Gravity, Urine	1.020			1.002 - 1.030	
pH, Urine	5.0			5.0 - 8.0	
Glucose, Urine	Normal			-	mg/dL
Ketones, Urine	Negative			-	
Leukocyte Esterase, Urine	Negative			-	
Nitrites, Urine	Negative			-	
Protein, Urine	Negative			-	

Investigator Signature: _____ Date: _____

Site: 1 Investigator: Kevin Biglan, MD
Coordinator: Panos Ginis

Clinically Significant: Please circle Y(Yes) or N(No)
Print Date: 02/05/2013 15:19 Original Print Date: 02/11/2010
New York State Dept. of Health No.: 33D1068640 CLIA: 33D1068640
Questions regarding reports: Please call 800-405-1889 / 585-350-2670 Page: 1 of 1

Review for Demographic Accuracy

Investigator Signature and Date

CS* is defined on the last page of the report as “Clinically Significant: Please circle Y(Yes) or N(No)”. It is up to the site investigator to determine whether the result is Clinically Significant.

Section 11. Data Queries

Data queries may be opened at sample accessioning in the laboratory for several reasons including but not limited to:

- Missing or incorrect specimens
- Damaged or incorrectly prepared samples
- Extra or unnecessary specimens
- Unlabeled or mislabeled specimens labeled with incomplete information
- Incomplete or indecipherable information recorded on the test requisition
- Discrepant demographic information provided
    - Test requisition compared to specimen tube labels
- Duplicate subject identifiers

These queries will be faxed to your site daily to the attention of the **Coordinator** and must be completed and returned within 2 business days. Some queries may delay reporting of laboratory results.

Data Inconsistencies Identified After Report Issuance

When the subject's visit report is received, it is important to review the subject demographic and visit information for accuracy. Some errors are not identifiable at the time of accessioning at the lab. For example, a unique subject identifier with the correct numbering scheme may have been recorded on the test requisition. It would have passed the edit checks at URMC Labs, but upon investigation turns out that it was the wrong identifier for the subject.

Should you discover an error when reviewing the report, you may either fax a request to make a correction and re-issue the report, or send an e-mail to the study support team. A data correction request form has been provided in the appendices of this manual for your use. If you e-mail the request, be sure to include the kit number of the order to be changed, the item to be changed, the item's current value, and the value that you would like to have the item corrected to.

Most changes are completed within one business day and a corrected report will be issued to your site after the correction is complete.

Data Queries Issued by CHET

At data lock or periodically throughout the study CHET will run edit programs to check for discrepancies between the lab data and the data recorded on the case report form. CHET may query the data and provide instruction directly to the laboratory to modify demographic and visit data. Based upon the sponsor's direction, corrected lab reports may be issued to your site.

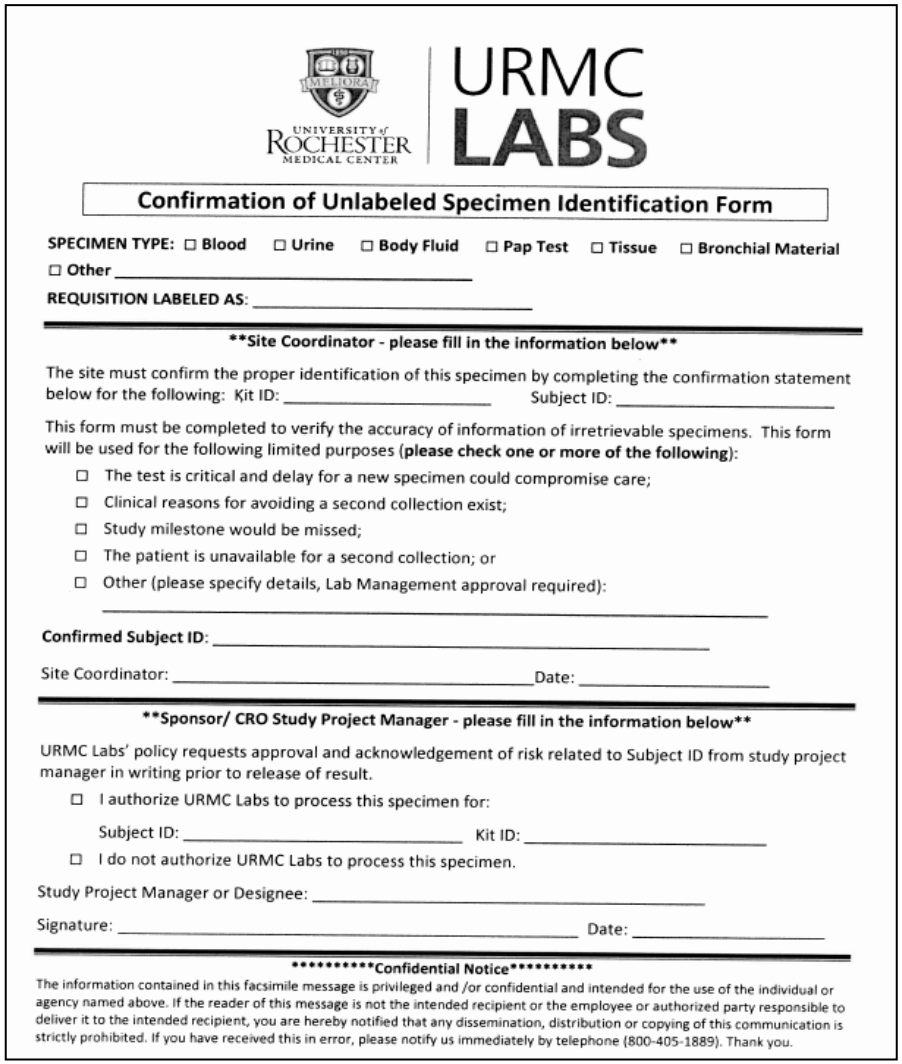
Section 11. Data Queries (Continued)

Directive if Specimens are Received Unlabeled

Specimens submitted to the laboratory for testing require complete and consistent labeling on the specimen and requisition. Specimens accompanied by a completed request form but received with partial or incomplete labeling or the reverse, specimens with complete labeling but with partial or incomplete request form, may be tested but results will be held until the missing information is obtained.

If the investigator site has retained a properly labeled back-up tube, the site may submit the back-up tube for testing. For specimens where time from collection may be critical to the integrity of analysis, the laboratory will determine if testing of the back-up tube can be completed based on specimen stability criteria.

Testing will not be performed on unlabeled (no identifiers) specimens, with the exception of irretrievable specimens. An irretrievable specimen is defined as "for those occasions where re-collection is not possible and the ordering physician or designee determines that analysis of the specific specimen submitted is critical to the care of the patient." The ordering physician or designee must accept responsibility for the specimen's identity in writing. The individual signing the form is assumed by the laboratory to have authority to make this decision. Approval and acknowledgement of risk from study project manager is required in writing prior to release of results. The Site coordinator and Study project manager will be asked to fill out the Confirmation of Unlabeled Specimen Identification Form (Seen on the right) prior to testing of the unlabeled specimen.



URMC LABS

Confirmation of Unlabeled Specimen Identification Form

SPECIMEN TYPE: ☐ **Blood** ☐ **Urine** ☐ **Body Fluid** ☐ **Pap Test** ☐ **Tissue** ☐ **Bronchial Material**
☐ **Other** _____

REQUISITION LABELED AS: _____

****Site Coordinator - please fill in the information below****

The site must confirm the proper identification of this specimen by completing the confirmation statement below for the following: Kit ID: _____ Subject ID: _____

This form must be completed to verify the accuracy of information of irretrievable specimens. This form will be used for the following limited purposes (**please check one or more of the following**):

- ☐ The test is critical and delay for a new specimen could compromise care;
- ☐ Clinical reasons for avoiding a second collection exist;
- ☐ Study milestone would be missed;
- ☐ The patient is unavailable for a second collection; or
- ☐ Other (please specify details, Lab Management approval required):

_____

Confirmed Subject ID: _____

Site Coordinator: _____ Date: _____

****Sponsor/ CRO Study Project Manager - please fill in the information below****

URMC Labs' policy requests approval and acknowledgement of risk related to Subject ID from study project manager in writing prior to release of result.

- ☐ I authorize URMC Labs to process this specimen for:

  Subject ID: _____ Kit ID: _____
- ☐ I do not authorize URMC Labs to process this specimen.

Study Project Manager or Designee: _____

Signature: _____ Date: _____

************Confidential Notice************

The information contained in this facsimile message is privileged and /or confidential and intended for the use of the individual or agency named above. If the reader of this message is not the intended recipient or the employee or authorized party responsible to deliver it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this in error, please notify us immediately by telephone (800-405-1889). Thank you.

Section 12. Frequently Asked Questions

This section is provided to address many common questions that arise to URMC Labs in conducting a study. However, this manual contains a significant amount of additional information regarding the lab services designed specifically for your study. It is recommended that you read the entire manual to obtain the most complete information.

Q: How can I order additional lab supplies?
A: Additional supplies may be requested by faxing a completed URMC Labs Kit Re-Supply Form to 585-486-1375 or email LabSRSS@urmc.rochester.edu. Supplies will arrive at your site within 7 to 10 business days. If you need supplies sooner than this, please call 800-405-1889 or 585-758-0525 to place your order.

Q: My copy of your lab licensure and accreditation is expiring. When will you send me an updated copy?
A: Historically, we do not receive an updated copy of our NYS license until 4 to 8 weeks after our inspection occurred. These inspections may not be conducted on an exact schedule and the current accreditation is considered valid until the inspection results are provided to us. The most current versions of our licensure and accreditation are also available in PDF format at the following web address: http://www.urmc.rochester.edu/urmc-labs/clinical/about-us/permits-certifications.aspx

Q: The patient was a difficult draw and I wasn't able to obtain the entire required specimen. What should I do?
A: Document the situation in the comments section of the test requisition and send everything that you could obtain. We will attempt to perform as much testing as possible from the available sample and notify you if any testing needs to be canceled.

Q: How do I order a test that isn't part of the study schedule?
A: Tests that are not part of the study must be done outside of the protocol through your own site's clinical lab. No additional testing may be requested through the study.

Q: My shipping address to receive supplies has changed. How can I relay the information?
A: Complete and submit the Site Information Change Form included in the appendices of your lab manual and in your initiation folder, by faxing to (585) 419-6115 or email to LabSRSS@urmc.rochester.edu.

Q: I haven't received a report for a lab visit that I collected. Where is it?
A: The report may not be available yet due to:

- Outstanding test results – Refer to Laboratory Report section for turnaround times
- The need to re-run and verify results
- An open data query

Section 12. Frequently Asked Questions (Continued)

Q: The investigator needs one of the test results right away. What should I do?
A: Contact URMC Labs at (800) 405-1889 or (585) 758-0525 to notify them of the situation. They will work with you to determine the soonest a result can be available and the best way to get the result to the investigator when it is.

Q: I have a patient with a scheduled lab visit that falls on a holiday. What should I do?
A: Contact the Project Manager at **CHET** to determine when you should collect the specimen. Refer to section 2 of this manual for information about holiday shipping.

Q: I can't find my copy of a test requisition for a kit that I shipped to the lab. How can I get a copy?
A: Contact URMC Labs by calling 800-405-1889 or emailing: LabSRSS@urmc.rochester.edu to request a copy of the requisition received by the laboratory.

Q: One of the tests that I sent to you was canceled due to hemolysis. How did that happen?
A: Hemolysis can be caused by several factors:

- Difficulty in obtaining blood from patient (hard draw)
- Prolonged Tourniquet use
- Use of too large or too small needle gauge for the patient
- Improper venipuncture
- Insufficient clot time prior to centrifugation
- Delay in sample separation
- Inadequate drying time after use of alcohol prep at draw site
- Vigorous shaking or mixing of the sample after draw
- Exposure to excessive heat or cold
- Patient health conditions, such as hemolytic anemia

Q: What is the difference between the Subject ID and the Kit ID on the labels?
A: The Subject ID is the number given to the patient at enrollment. The site must fill out the subject ID on the tubes and the test requisition. The Kit ID is a unique number for each kit provided by URMC Labs at time of kit build, and is associated with one subject and visit. This number will be entered into a database that allows us to document the subject demographics as well as collection information for that particular subject/visit. To make sure our records are consistent with yours, please only use one set of labels with one unique Kit ID per visit/subject.

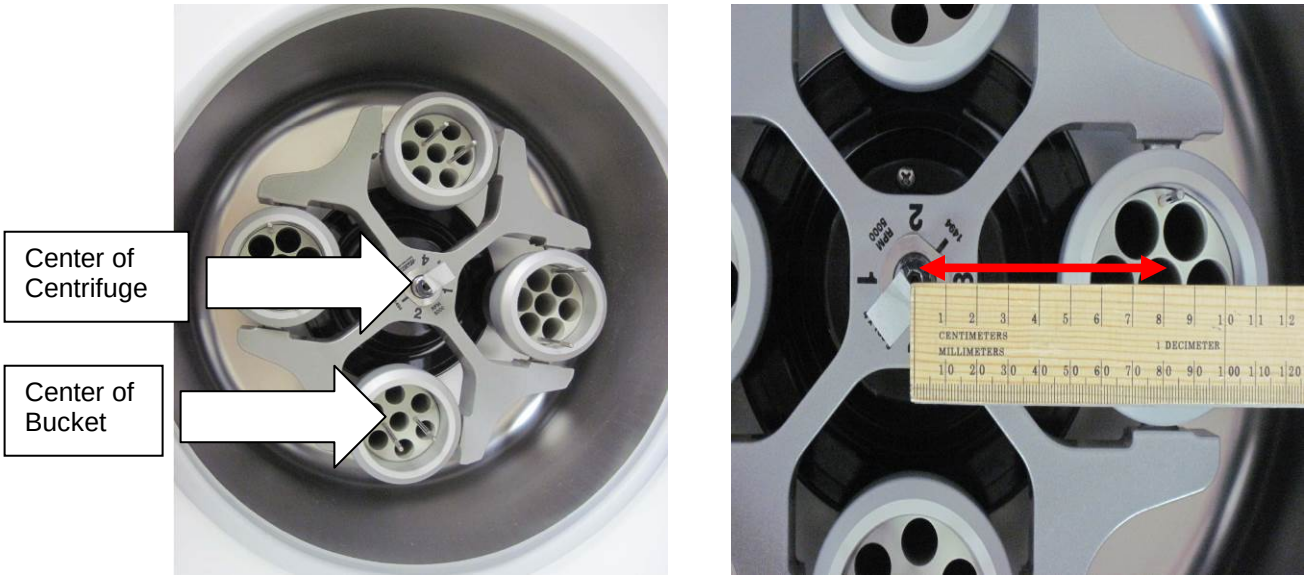
Q: Will we receive the UN1845, UN3373, and Biohazard labels for shipping?
A: All URMC shipping boxes are pre-printed with the UN3373 label and have biohazard labels on them. The Frozen shipping boxes are also pre-printed with the UN1845 label. URMC Labs provides all IATA compliant supplies (except dry ice) and labels needed for shipping. The sites are only required to fill out the package and sender information on the FedEx waybill and on the outside of the shipping box (for frozen/combo shipments).

Section 12. Frequently Asked Questions (Continued)

Q: How can I calculate the g force of my centrifuge?

A: If you do not have your centrifuge manual or your manual does not have a conversion chart then you need to determine the radius of your centrifuge.

- Place one edge of the ruler (metric side up) at the center of the centrifuge and measure to the center of the sample bucket or tube.
- In the photograph on the right the radius is 8 cm from center of the rotor to center of the sample bucket.



- Using the conversion table below; if the radius for the centrifuge is 8 cm, set the centrifuge speed (rpm) at 4095 or 4100 for a speed of 1500 x g.

Conversion Table for 1500 x g (CHANGE IF OTHER THAN 1500 X g)

Radius	Speed (rpm)*
6	4729
7	4378
8	4095
9	3861
10	3663
11	3492
12	3343
13	3213
14	3096
15	2991
16	2896
17	2809

*Round up or down depending on centrifuge range

Section 12. Frequently Asked Questions (Continued)

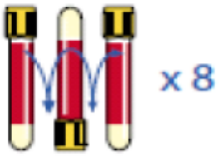
Q: How can I tell if the SST is correctly centrifuged and separated?

How to Prepare a Quality Sample

- Before use, tube should be stored at 4-25°C (39-77°F)
- It is recommended that the serum be physically separated from contact with the cells as soon as possible with a **Maximum time limit of 2 hours from the time of collection**

1) Mix the Sample

Mix the tube by **8 to 10 complete inversions**



*Mixing is critical to achieving appropriate clotting times and clot formation. Inadequate mixing may result in incomplete clotting

2) Allow blood to Clot

Allow tube to clot at room temperature in a vertical position for **At Least 30 Minutes**

*Insufficient clotting (short clotting time) can result in the formation of fibrin, which may interfere with barrier formation.

*Samples from certain populations of patients with impaired coagulation may require longer than 30 minutes to clot:

- Blood from patients on anticoagulant therapy or with certain diseases (e.g., liver disease) may require longer clotting time.

-Blood from patients on high doses of heparin may not clot at all

-Multiple Myeloma: the isolated myeloma globulin inhibits all 3 stages of fibrin formation.

3) Centrifugation

Horizontal (Swing-Bucket) Centrifuge:

Centrifuge at 1500 x g for 10 minutes

Fixed-Angle Centrifuge:

Centrifuge at 1500 x g for 15 minutes

*Flow properties of barrier material are temperature dependent! Gel flow may be impeded if chilled before centrifugation. For optimal flow and centrifugation, set refrigerated centrifuge to 25°C (77°F)

Section 13. Required Documentation and Licensure

- Reference Ranges
- Medical Director's Curriculum Vitae
  -James P. Corsetti, MD, PhD
- Medical Director's License
  -James P. Corsetti, MD, PhD
- CAP Accreditation(s)
  -URMC Labs
  77 Ridgeland Rd
  Rochester NY 14623
- Laboratory Licensure and Certification(s)
  -URMC Labs
  77 Ridgeland Rd
  Rochester NY 14623

  -All Permits and Certifications are available online:
  http://www.urmc.rochester.edu/urmc-labs/clinical/about-us/permits-certifications.aspx

Section 14. Material Safety Data Sheets

- Alcohol Pads
- Lavender EDTA Tubes
- 5mL Gold top SST
- 3mL Green Na Heparin
- 8.5mL Yellow ACD
- Urinalysis Preservative