


# THERAPEUTIC DRUG MONITORING PROCESS

## Considerations for Using Therapeutic Drug Monitoring

Providers may order drug levels on tuberculosis patients not responding to adequate therapy, or those with risk factors for poor absorption. Testing is performed at the University of Florida's Infectious Disease Pharmacokinetics Laboratory (IDPL). DSHS will cover the cost of drug levels based on below criteria. Programs may draw drug levels using funds outside of the TB and Hansen's Disease Branch if requests fall outside this criteria.

Note: Only rifamycin and isoniazid levels will be covered, unless patient is on second-line medications or a consultation from a DSHS-recognized TB medical consultant recommends otherwise.



### Criteria\* for Collecting Serum Drug Levels

<b>Bacteriological Criteria</b> (consider at 8 weeks of therapy)	<b>Medical Criteria</b> (consider at 2-4 weeks of therapy)	<b>Clinical Criteria</b> (consider at 8 weeks of therapy)	<b>Criteria based on TB Diagnosis**</b>
<p>Slow response to adequate therapy at <b>8 weeks</b> of treatment, evidenced by the following:</p> <ul style="list-style-type: none"> <li>• Patient remains AFB sputum smear positive 2+ or greater (unless easily explained)</li> </ul> <p>And/or</p> <ul style="list-style-type: none"> <li>• Sputum smear results not decreasing as expected (4+ to 3+, 2+, etc.)</li> </ul>	<ul style="list-style-type: none"> <li>• TB/poorly controlled diabetes comorbidity</li> <li>• Mal-absorption due to chronic or acute co-morbidity</li> <li>• Chronic or excessive vomiting or diarrhea</li> <li>• HIV infection and CD-4 count &lt;100**</li> <li>• Low or high body mass index (&gt;10% above or below ideal body weight)</li> </ul>	<ul style="list-style-type: none"> <li>• No improvement of TB symptoms (i.e. no weight gain, no reduction in cough, etc.) at 8 weeks</li> <li>• Worsening CXR anytime during course of adequate therapy</li> <li>• New clinical deterioration, likely related to TB (i.e. new evaluation for TB relapse or concern for drug resistance**)</li> </ul>	<ul style="list-style-type: none"> <li>• Patient Relapse: When signs and symptoms of TB return within two years of a prior episode of disease and there was a good possibility that relapse was due to low drug levels (exclude previous poor adherence, missed doses, or N/V)</li> <li>• When second line drugs need monitoring, as per consult recommendations</li> <li>• TB meningitis</li> </ul>

\* **Therapeutic Drug Monitoring should be reserved for patients who are not responding to adequate therapy**, and not necessarily for patients who meet some of the stated criteria and are otherwise doing well.

\*\* Consultation recommended by a DSHS-recognized TB medical consultant, see list here: [dshs.texas.gov/idcu/disease/tb/consultants/](https://dshs.texas.gov/idcu/disease/tb/consultants/)

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### Supplies Needed

TB programs may need to purchase additional supplies for collecting and shipping.



- ❑ **Plain red top tubes:** These cannot be used from the DSHS state laboratory, as the state lab does not process the test.



- ❑ **Pipettes:** For aliquoting serum from the red top tubes into polypropylene tubes.



- ❑ **Polypropylene tubes:** Used for the aliquoted serum that will be frozen and shipped.



- ❑ **Dry Ice:** Must be purchased locally; typically found at local grocery stores. Five pounds (5lbs) is required for shipping.



- ❑ **Cold Boxes:** A vaccine-size cold box is recommended.



- ❑ **Labels:** Biological Substances Category B Label UN 3373 and Dry Ice Label UN 1845



- ❑ **IDPL Laboratory Requisition:** See page 6 for details

## THERAPEUTIC DRUG MONITORING PROCESS

### Prepare for Specimen Collection

Review IDPL requisition for specimen collection times:  
[idpl.pharmacy.ufl.edu/forms-and-catalog/idpl-requisition/](http://idpl.pharmacy.ufl.edu/forms-and-catalog/idpl-requisition/)

Review specimen shipping and collection details:  
[idpl.pharmacy.ufl.edu/forms-and-catalog/sample-handling-instructions/](http://idpl.pharmacy.ufl.edu/forms-and-catalog/sample-handling-instructions/)

### Step 1

**Perform Directly Observed Therapy (DOT) of TB medications being tested, ensuring that the blood draw can occur at the indicated time *after* the dose of medication is observed.**

The number of hours after the dose to draw the samples are shown in parentheses after each drug on the IDPL requisition. It shows the peak time of absorption first and then 4 hours post peak, which may help indicate if there is delayed absorption.

Providers may choose to collect a peak, or both peak and post-peak levels. When collecting post-peak levels, and it is not possible to collect at 4 hours after the first draw, consideration may be made to shorten to at least 2 hours after peak (i.e. collect at 4 hours after DOT). Consult with the ordering physician first to determine which levels are needed; IDPL staff may serve as a resource for drug and patient-specific questions by phone (352) 273-6710 or email [peloquinlab@cop.ufl.edu](mailto:peloquinlab@cop.ufl.edu).

*For example: If testing both rifampin and isoniazid peak levels, DOT would be provided, and a peak level would be drawn at 2 hours after DOT. A second draw may also be recommended 6 hours after DOT for a post-peak level. Ensure a new laboratory requisition is completed for each timed draw.*

INH	Isoniazid (1-2 H & 6 H)
RZAP	Rythazamide (2 H & 6 H)
RBN	Rifabutin (3 H & 7 H)
RIFN	Rifampin (2 H & 6 H)
RILP	Rilpivirine (trough & 4-5H)
VORL	Voriconazole (trough & 2 H)

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### Step 2

**Perform phlebotomy and collect *at least* 1 mL of blood per drug to be tested in a plain Red Top tube.**

- Required volume of serum once blood is centrifuged is *at least* 0.5 mL.
- Document timing of the blood draw on the requisition; include time DOT was provided.
- Use a separate tube for each test. (*Consider drawing an extra tube to freeze serum and save if needed.*)

### Step 3

**Centrifuge blood and aliquot the separated serum into a labeled polypropylene or similar plastic tube, using one tube per test; or, coordinate processing with a local laboratory.**

- Draw blood, allow 20 minutes to clot, and then centrifuge. Centrifuging should occur within 2 hours of collection. If blood will be processed in a local laboratory and not by collector, it can be kept on ice while in transport. Coordinate with the lab to ensure timely processing.
- A pipette can be used to harvest out the separated serum and aliquot into the polypropylene tube.
- Label the tube with patient name, date of birth, date/time of collection, and drugs to be tested.

### Step 4

**Keep separated serum frozen (or refrigerated until it can be frozen) to prepare for shipping.**

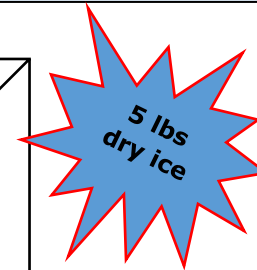
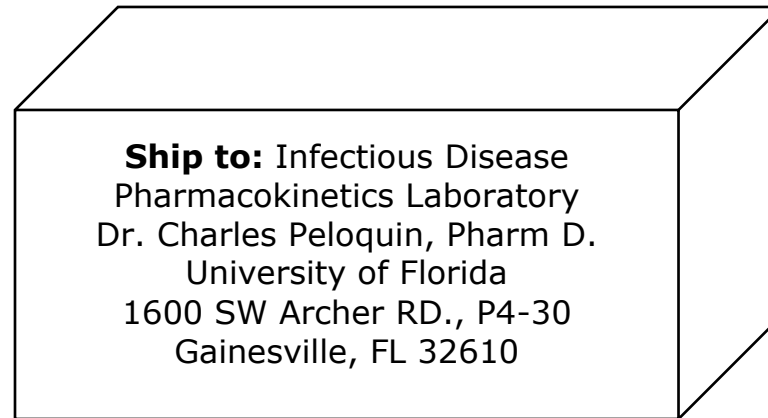
- Freeze at -70C if possible, but at minimum -20C. Serum that is frozen above -20C is stable for 31 days.
- If an ultralow freezer is unavailable, the serum can be frozen in a regular freezer; do not allow it to go through a defrost cycle.
- Alternately, the tube with decanted serum can be placed on a rack and stored on dry ice (the rack should prevent direct contact between the tube and the ice; the serum will slowly freeze without being shocked by contact with the dry ice).

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### Shipping Details

- Place samples in zip-lock plastic bags and pack upright in Styrofoam boxes with 5 lbs. of dry ice.
  - Pack properly for Biological B specimen and dry ice shipping
  - Refer to DSHS *Tuberculosis Specimen Shipping Guide* for details:  
[dshs.texas.gov/IDCU/disease/tb/policies/TBSpecimenShippingGuide.pdf](https://dshs.texas.gov/IDCU/disease/tb/policies/TBSpecimenShippingGuide.pdf)

Ship to:



- Severe hemolysis
- Thawed samples for greater than 6-24 hours, depending on drug being tested
- Incomplete laboratory requisition

### Receiving Results and Interpretations

The treating provider will determine if medication dosages will need to be changed based on the results of the serum drug level testing. Each result will be interpreted by Charles Peloquin, Pharm D, at the IDPL who may also be consulted *upon request*. Contact [peloquinlab@cop.ufl.edu](mailto:peloquinlab@cop.ufl.edu), phone: (352) 273-6710.

# THERAPEUTIC DRUG MONITORING PROCESS

## INFECTIOUS DISEASE PHARMACOKINETICS LABORATORY

1600 SW Archer Rd., P4-30  
Gainesville, FL 32610  
Phone: 352-273-6710 Fax: 352-273-6804  
E-mail: [peloquinlab@cop.ufl.edu](mailto:peloquinlab@cop.ufl.edu)  
Website: <http://idpl.pharmacy.ufl.edu>



**Fill out entire top portion with patient and TB clinic details**

Patient Last, First Name, M.I. (Required)			<input type="checkbox"/> Male <input type="checkbox"/> Female	Mail results to: (Required)
Date of Birth:	Patient ID:			
Referring Physician (Required):	Physician NPI #	Physician Phone #		
Fax #	Facility Phone #			
<b>COMPLETE SECTION BELOW ONLY IF BILLING INFORMATION DIFFERS FROM "MAIL RESULTS TO" INFORMATION</b> Please note: We do not bill 3 <sup>rd</sup> party payers. The laboratory or office shipping the samples accepts responsibility for payment.				
Bill to / Contact Name:				
Billing Address:				
City		State	Zip	
Telephone #				

**Include clinic address and fax number to receive results**

**Contact the DSHS TB and Hansen's Disease Branch for billing information:**

- [TBProgram@dshs.texas.gov](mailto:TBProgram@dshs.texas.gov)
- Phone: (737) 255-4300

(Please submit a separate requisition for each sample collection time) All results are reported within 7 days of receiving specimen.  
Specimen source (circle one): serum      cerebrospinal fluid      other: \_\_\_\_\_

REQUIRED	Drug 1	Drug 2	Drug 3	Drug 4
Drug name to be Assayed				
ICD Code or Diagnosis				
Drug Dose (mg) (Specify: PO, IV, IM)				
# Doses per week				
Date of last dose				
Time of last dose (For IV: Start/End)				
Date blood drawn				
Time blood drawn				

**Complete all fields for each drug to be tested**

The number of hours after the dose to collect concentrations are shown in parentheses after each drug name below. To test for delayed drug absorption, a second sample should be collected 4 hours after the "peak". **Trough concentrations (prior to next dose) are recommended for the anti-HIV and anti-fungal drugs.**

Drug(s) to be assayed (provide 2 ml serum per test)

AZL	Azithromycin (2-3 H & 6-7 H)	ETAH	Ethionamide (2 H & 6 H)	PZAH	Pyrazinamide (2 H & 6 H)		β-Lactams (intravenous doses)
BDQ	Bedaquiline (5 H & 24 H)	INH	Isoniazid (1-2 H & 6 H)	RBN	Rifabutin (3 H & 7 H)		β-Lactams, post intravenous & trough
CIPH	Ciprofloxacin (2 H & 6 H)	ITRL	Itraconazole (trough & 3-4 H)	RIFH	Rifampin (2 H & 6 H)	AMOX	Amoxicillin
CLART	Clarithromycin (2-3H&6-7 H)	LFLHL	Levofloxacin (2 H & 6 H)	RILP	Rilpivirine (trough & 4-5H)	AMPI	Ampicillin
CFH	Clofazimine (2-3 H & 6-7 H)	LNZL	Linezolid (trough, 2 & 5-6 H)	VORL	Voriconazole (trough& 2 H)	AZTRE	Aztreonam
CSH	Cycloserine (2-3 H & 6-7 H)	LOPV	Lopinavir (trough & 4-6H)			CEFAZ	Cefazolin
DARU	Darunavir (trough & 2-4 H)	MXFL	Moxifloxacin (2 H & 6 H)			CEFE	Cefepime
DTG	Dolutegravir (trough & 2 H)	PASH	p-Aminosalicylic acid (6H)	NAFC	Nafcillin	CEFT	Ceftriaxone
EVL	Efavirenz (trough & 5 H)	PMD	Pretomanid (5 H & 24 H)	MERO	Meropenem	IMIP	Imipenem
EMBH	Ethambutol (2-3 H & 6-7 H)	POSA	Posaconazole (trough& 3H)	PIPE	Piperacillin	OXA	Oxacillin

**Circle which level was collected (i.e. 2H or 6H)**

**Sample preparation and shipment:** Collect in a plain red top, 5 ml tube. Allow the sample to clot and separate serum from cells by centrifugation and aliquot into a labeled polypropylene or similar plastic tube. Use a separate tube for each test ordered. Allow room for expansion of sample inside tube. Freeze at -70°C if possible (otherwise -20°C.) Ship by overnight delivery on 2.5 lbs. dry ice. **SHIP SAMPLES TO BE RECEIVED MONDAY THROUGH FRIDAY, DO NOT SHIP ON FRIDAY OR SATURDAY.**

List other medications patient is currently taking: \_\_\_\_\_

For UFL Use Only

Date Received: \_\_\_\_\_  
Time Received: \_\_\_\_\_  
Condition: (circle one)  
Frozen      Partially Frozen      Thawed

**List any other medication the patient is taking, as they may impact the interpretations**