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

<table>
<thead>
<tr>
<th>Bacteriological Criteria (consider at 8 weeks of therapy)</th>
<th>Medical Criteria (consider at 2-4 weeks of therapy)</th>
<th>Clinical Criteria (consider at 8 weeks of therapy)</th>
<th>Criteria based on TB Diagnosis**</th>
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</thead>
<tbody>
<tr>
<td>Slow response to adequate therapy at 8 weeks of treatment, evidenced by the following:</td>
<td>• TB/poorly controlled diabetes comorbidity</td>
<td>• No improvement of TB symptoms (i.e. no weight gain, no reduction in cough, etc.) at 8 weeks</td>
<td>• 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)</td>
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<tr>
<td>• Patient remains AFB sputum smear positive 2+ or greater (unless easily explained)</td>
<td>• Mal-absorption due to chronic or acute co-morbidity</td>
<td>• Worsening CXR anytime during course of adequate therapy</td>
<td>• When second line drugs need monitoring, as per consult recommendations</td>
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<tr>
<td>And/or</td>
<td>• Chronic or excessive vomiting or diarrhea</td>
<td>• New clinical deterioration, likely related to TB (i.e. new evaluation for TB relapse or concern for drug resistance**)</td>
<td>• TB meningitis</td>
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<tr>
<td>• Sputum smear results not decreasing as expected (4+ to 3+, 2+, etc.)</td>
<td>• HIV infection and CD-4 count &lt;100**</td>
<td></td>
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</tr>
</tbody>
</table>

* 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/
THERAPEUTIC DRUG MONITORING PROCESS

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/

Review specimen shipping and collection details:
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 peloquinnlab@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.
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).
**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](dshs.texas.gov/IDCU/disease/tb/policies/TBSpecimenShippingGuide.pdf)

**Ship to:**
**Infectious Disease Pharmacokinetics Laboratory**  
Dr. Charles Peloquin, Pharm D.  
University of Florida  
1600 SW Archer RD., P4-30  
Gainesville, FL 32610

**STOP**  
**Unacceptable Conditions**
- 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, phone: (352) 273-6710.
**THERAPEUTIC DRUG MONITORING PROCESS**

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

*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*

*Complete all fields for each drug to be tested*

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

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