# Therapeutic Drug Monitoring Process

## 1. Verify or request order for collecting serum drug levels

Criteria* for Considering Therapeutic Drug Monitoring on TB patients

<table>
<thead>
<tr>
<th>Bacteriological Considerations</th>
<th>Medical Considerations</th>
<th>Clinical Considerations</th>
<th>Considerations based on TB Diagnosis**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow response to adequate therapy at 4-8 weeks of treatment, evidenced by the following:</td>
<td>• TB/diabetes comorbidity: Serum drug levels can be drawn two weeks after initiation of adequate therapy</td>
<td>• No improvement or worsening of TB symptoms (i.e. no weight gain, no reduction in cough, etc.)</td>
<td>• Patient Relapse: When signs and symptoms of TB return within two years of a prior episode of disease; serum drug levels can be drawn two weeks after initiation of therapy</td>
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<tr>
<td>• Patient remains AFB sputum smear positive at 4-8 weeks, and/or</td>
<td>• Mal-absorption due to chronic or acute comorbidity</td>
<td>• Worsening CXR anytime during course of adequate therapy</td>
<td>• When second line medications need monitoring (i.e. Cycloserine, which has a narrow therapeutic range and potential for toxicity)</td>
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<tr>
<td>• Sputum smear results not decreasing adequately (4+ to 3+, 2+ to 1+, etc.)</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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<td>• HIV infection and CD-4 count &lt;100**</td>
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<td>• Low or high body mass index (&gt;10% above or below ideal body weight)</td>
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</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 Medical Consultant, see list here:[http://www.dshs.texas.gov/idcu/disease/tb/consultants/](http://www.dshs.texas.gov/idcu/disease/tb/consultants/)
2. Contact the DSHS TB and Hansen’s Disease Branch for billing instructions

First time submitters: Contact the TB and Hansen’s Disease Branch, either via email elizabeth.foy@dshs.texas.gov, fax written request to 512-533-3167 attention: TB and Hansen’s Disease Branch, or call the Branch at 512-533-3000 and ask for the TB Program staff. Once completed, the submitter will be sent the National Jewish Laboratory Requisition which includes DSHS Billing Information.

3. Arrange timing of the blood draw and directly observed therapy (DOT) according to which drug/s are being tested

Steps to collecting serum drug levels

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.

- Timing of draws per drug can be found on the National Jewish Laboratory requisition*. Time of dose and draw must be written on form.

* The requisition states the name of the drug and hour duration of when to draw the peak level, i.e. "Rifabutin 3h". If peak Rifabutin levels were being tested, the DOT provider would observe the patient taking their current dose of Rifabutin, wait three (3) hours, and draw the blood as specified.
THERAPEUTIC DRUG MONITORING PROCESS

Step 2

Perform phlebotomy and collect blood in an 8-10 ml plain Red Top tube. (Also acceptable is an 8-10 ml Green Top tube, but it is not preferred.)

- Preferred volume is at least 2 ml of serum per test for adults, 0.5 ml for pediatrics.
- Document timing of the blood draw on the requisition.
- Use a separate tube for each test ordered. Allow room for expansion of sample.

Step 3

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

- Centrifuging should occur within 2 hours of collection, preferred in 30 mins. Draw blood, allow 20 minutes to clot, and then centrifuge. If blood will be processed in a local laboratory and not by collector, it can be kept on ice while in transport. Coordinate with lab to ensure timely processing.
- A pipette can be used to aliquot separated serum into the polypropylene tube.
- The 50ml conical tubes for sputum collection are made of polypropylene and can be used for decanted serum.

Step 4

Ensure separated serum is frozen (or kept refrigerated until freezing) to prepare for shipping.

- Freeze at -70C if possible, but at minimum -20C.
- 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).
4. Send/Ship Serums to National Jewish Laboratory

Fully complete the National Jewish Laboratory Requisition. Include:
- Drug dosage, frequency, method of administration, and date and time of last dose prior to draw

Ship samples via overnight delivery on at least 3 lbs of dry ice.
- Ship samples to be received Monday through Friday
- Do not ship on Friday or Saturday, or the day prior to a holiday
- Package properly for dry ice handling*, including using a dry-ice specific label, and a return label for box to be shipped back to sender

*Not all couriers will ship dry ice, check before sending. Full shipping guidelines can be found on the National Jewish website: https://www.nationaljewish.org/for-professionals/diagnostic-testing/adx/diagnostic-testing/shipping-guidelines

Ship to:
National Jewish Health
Pharmacokinetics Laboratory
1400 Jackson Street, K425
Denver, CO 80206
STOP
Unacceptable Conditions

- Severe hemolysis
- Thawed samples for greater than 6-24 hours, depending on drug being tested - ensure serum is shipped on at least 3 lbs dry ice
- Incomplete laboratory requisition

5. Respond to results as appropriate

Treating provider will determine if medication dosages will need to be changed based on the results of the serum drug level testing

Request consult if needed
Consultation recommended by a DSHS recognized Medical Consultant, see list here: http://www.dshs.texas.gov/idcu/disease/tb/consultants/
**Billing Information:** Request from DSHS Tuberculosis and Hansen’s Disease Branch (see page 2 of process).

**Report Delivery Information:** Local (LHD) or Regional Health Department (HSR) information here. **Make sure fax number is correct** to ensure results are returned to sender.

**Submitter Specimen #:** Can be any ID that the LHD or HSR uses to identify patient specimen; leave blank if none.

**Submitted By:** place the name of the LHD or HSR contact person (i.e. Nurse Case Manager for the patient). Also include contact # of the submitter.

All other sections must be filled out, including patient information, which drugs are being tested, times of dosing, etc.
Additional Resources

National Jewish Laboratory Requisition:

Instructions per drug (type in drug name being tested in Search box):
https://www.nationaljewish.org/for-professionals/diagnostic-testing/adx/search-adx-tests?ref=bottom

Shipping Guidelines:
https://www.nationaljewish.org/for-professionals/diagnostic-testing/adx/diagnostic-testing/shipping-guidelines

DSHS Recognized Medical Consultants:
http://www.dshs.texas.gov/idcu/disease/tb/consultants/