

THERAPEUTIC DRUG MONITORING PROCESS

1. Verify or request order for collecting serum drug levels



Providers may order drug levels on tuberculosis patients not responding to adequate therapy, or those with risk factors for poor absorption. 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 rifamycins and isoniazid **peak** levels will be covered, unless patient is on second-line medications; consultation from a DSHS-recognized Medical Consultant may be needed.



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

* **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/>

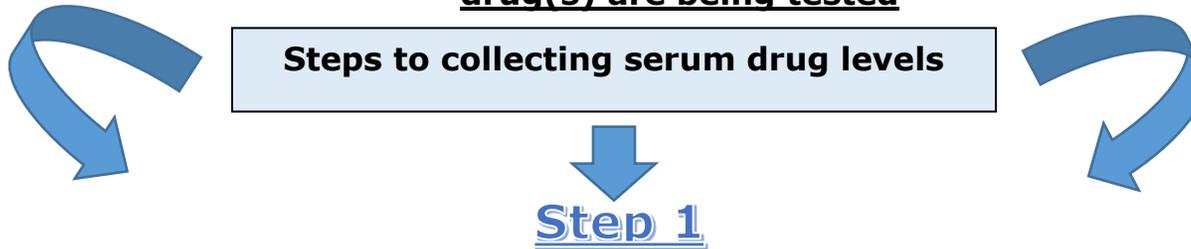
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2. Contact the DSHS TB and Hansen’s Disease Branch for billing instructions



First-time users may contact the TB and Hansen’s Disease Branch at 512-533-3000 and ask for the TB Program administrative or nursing staff. You will be sent the ***National Jewish Laboratory Requisition*** which includes DSHS Billing Information. This may be saved and used again for subsequent draws without contacting the Branch, ***unless criteria for drawing drug levels falls outside the requirements on page 1.***

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



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 the form. In general, 2-hour levels are typically collected unless otherwise stated on the requisition (i.e. rifabutin is 3 hrs) or if there is a high likelihood of slow absorption or rapid metabolism; in that instance (when testing for delayed drug absorption), a second sample should be collected 4 hours after the specified “peak”.

* *The requisition states the name of the drug and hour duration of when to draw the peak level, i.e. “Rifampin (2h)”. If peak Rifampin levels were being tested, the DOT provider would observe the patient taking their current dose of Rifampin, wait two (2) hours, and draw the blood as specified.*

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rs after the dose to collect “peak” concentrations is shown in parentheses after each drug name and sample may be collected 4 hours after the “peak”. Trough concentrations (prior to next dose) are recommended for the anti-HIV and anti-fungal drugs.				
rif (2-4h)	<input type="checkbox"/> LFLHL	Levofloxacin (2h)	<input type="checkbox"/> RBN	Rifabutin (3h)
line (2h)	<input type="checkbox"/> LNZZL	Linezolid (2h)	<input type="checkbox"/> RIFH	Rifampin (2h)
- (2h)	<input type="checkbox"/> LOPV	Lopinavir (4-6h)	<input type="checkbox"/> DEPTAL	- (2h)

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Step 2

Perform phlebotomy and collect 4-6 ml of 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 of *serum* once blood is centrifuged is at least 2 ml 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. (*Consider drawing an extra tube to freeze serum and save if needed.*)

Step 3

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

- Draw blood, allow at least 30 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 lab to ensure timely processing.
- A pipette can be used to aliquot separated serum into the polypropylene tube.

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).

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4. Send/Ship Serums to National Jewish Laboratory

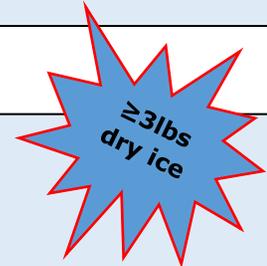
Fully complete the National Jewish Laboratory Requisition. Include:

- 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 pounds 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



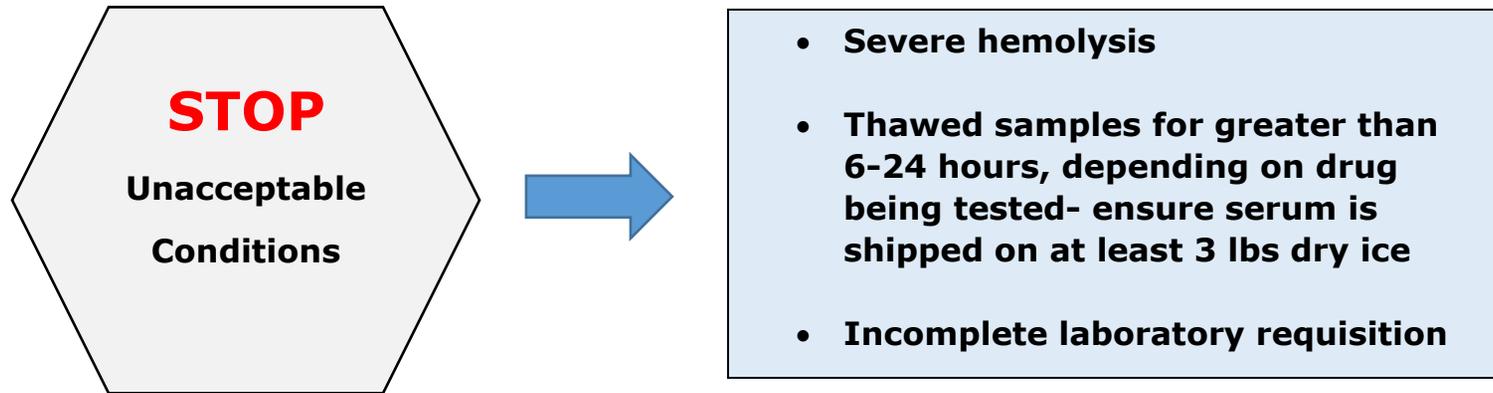
**Not all couriers will ship dry ice, check before sending. Full shipping guidelines can be found on the National Jewish website:
<https://www.nationaljewish.org/for-professionals/diagnostic-testing/adx/diagnostic-testing/shipping-guidelines>*



Ship to:

National Jewish Health
Pharmacokinetics Laboratory
1400 Jackson Street, K425
Denver, CO 80206

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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 TB Consultant, see list here: <http://www.dshs.texas.gov/idcu/disease/tb/consultants/>

THERAPEUTIC DRUG MONITORING PROCESS

Advanced Diagnostic Laboratories National Jewish Health® SHIP TO: National Jewish Health
Pharmacokinetics Laboratory | 800.550.6227 | 303.270.2175 fax | njlabs.org Pharmacokinetics Laboratory
Pharmacokinetics Diagnostics Requisition 1400 Jackson Street, K425
Denver, CO 80206

Assays may require up to seven business days for completion. Please submit a separate requisition for each sample collection time.

1. PATIENT INFORMATION							
Patient Name (Last, First)		<input type="checkbox"/> Male <input type="checkbox"/> Female DOB: / /					
2. BILLING INFORMATION - INSTITUTIONAL BILLING ONLY		3. REPORT DELIVERY INFORMATION					
National Jewish Health Advanced Diagnostic Laboratories does not bill patients directly or third-party health insurance. Visit njlabs.org or call for details.		Client ID					
Client ID		Account Name					
Account Name		Address					
Address		City		State Zip			
City		Phone		Secure Fax			
State Zip		<input type="checkbox"/> Duplicate Report Request Attn:					
Phone		Phone		Secure Fax			
Fax		Phone					
4. SPECIMEN INFORMATION							
Submitted By		Phone		Submitter Specimen #			
Specimen Source							
Required	Drug 1	Drug 2	Drug 3	Drug 4			
Drug name to be tested							
Specimen (Serum, CSF, Plasma, Other)							
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							
5. THERAPEUTIC DRUG MONITORING							
Please provide 2 mL serum per test. The number of hours after the dose to collect "peak" concentrations is shown in parentheses after each drug name, if applicable. To test for delayed drug absorption, a second sample may be collected 4 hours after the "peak". Trough concentrations (prior to next dose) are recommended for the anti-HIV and anti-fungal drugs.							
<input type="checkbox"/> PKABC	Abacavir (1-2h)	<input type="checkbox"/> PKDRV	Darunavir (2-4h)	<input type="checkbox"/> PKLZD	Linezolid (2h)	<input type="checkbox"/> PKRAL	Raltegravir (3h)
<input type="checkbox"/> PKAMX	Amoxicillin	<input type="checkbox"/> PKDLV	Delavirdine (2h)	<input type="checkbox"/> PKLPV	Lopinavir (4-6h)	<input type="checkbox"/> PKRFB	Rifabutin (3h)
<input type="checkbox"/> PKAPV	Amprenavir (2-3h)	<input type="checkbox"/> PKEFV	Efavirenz (5h)	<input type="checkbox"/> PKMPK	12hr Methylprednisolone Study	<input type="checkbox"/> PKRIF	Rifampin (2h)
<input type="checkbox"/> PKATV	Afazanavir (2h)	<input type="checkbox"/> PKFTC	Emtricitabine (1-2h)	<input type="checkbox"/> PKMXF	Moaxifloxacin (2h)	<input type="checkbox"/> PKRFP	Rifapentine (5h)
<input type="checkbox"/> PKAZM	Azithromycin (2-3h)	<input type="checkbox"/> PKEMB	Ethambutol (2-3h)	<input type="checkbox"/> PKNFV	Nelfinavir (2-3h)	<input type="checkbox"/> PKRTV	Ritonavir (2-3h)
<input type="checkbox"/> PKCFZ	Clofazamine (2-3h)	<input type="checkbox"/> PKETA	Ethionamide (2h)	<input type="checkbox"/> PKNVP	Nevirapine (2h)	<input type="checkbox"/> PKSQV	Saquinavir (2-3h)
<input type="checkbox"/> PKCLR	Clarithromycin (2-3h)	<input type="checkbox"/> PKFLC	Fluconazole (2h)	<input type="checkbox"/> PKOFK	Ofloxacin (2h)	<input type="checkbox"/> PKSLI	Sildenafil (1-2h)
<input type="checkbox"/> PKCM	Capreomycin (1-2h)	<input type="checkbox"/> PKIDV	Indinavir (1-2h)	<input type="checkbox"/> PKPAS	P-Aminosalicylic Acid (6h)	<input type="checkbox"/> PKD4T	Stavudine (1h)
<input type="checkbox"/> PKCIP	Ciprofloxacin (2h)	<input type="checkbox"/> PKINH	Isoniazid (1-2h)	<input type="checkbox"/> PKPOS	Posaconazole (3-6h)	<input type="checkbox"/> PKSM	Streptomycin (1-2h)
<input type="checkbox"/> PKCRT	Cortisol (random)	<input type="checkbox"/> PKITC	Itraconazole (3-4h)	<input type="checkbox"/> PKCFK	12 hr Prednisolone Study	<input type="checkbox"/> PKTPV	Tipranavir (3h)
<input type="checkbox"/> PKSTM	Cortisol Adrenal Stimulation	<input type="checkbox"/> PK3TC	Lamivudine (1h)	<input type="checkbox"/> PKPDK	6 hr Prednisolone Study	<input type="checkbox"/> PKVRC	Voriconazole (2h)
<input type="checkbox"/> PKCSH	CycloSERINE (2-3h)	<input type="checkbox"/> PKLVX	Levofloxacin (2h)	<input type="checkbox"/> PKPZA	Pyrazinamide (2h)		
6. SPECIAL INSTRUCTIONS							
Please list additional medications patient is currently taking:							
Sample preparation and shipment: Collect in a plain red top, 8-10 mL tube. Allow to clot for 30 minutes, separate serum from cells immediately 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 on ≥ 3 lbs. dry ice via overnight transport. SHIP SAMPLES TO BE RECEIVED MONDAY THROUGH FRIDAY. DO NOT SHIP ON FRIDAY OR SATURDAY.							
INTERNAL USE							
Received By	Date	Time	Condition:	<input type="checkbox"/> Frozen: <input type="checkbox"/> Ref <input type="checkbox"/> Thawed			

6278.261017-ADK ADxReq-07 PK (10/01/2018)

Billing Information: Request from DSHS Tuberculosis and Hansen's Disease Branch if you do not have the requisition with this information already (see page 2 of process).

Report Delivery Information: Local Health Department (LHD) or Public Health Region (PHR) 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 PHR uses to identify patient specimen; leave blank if none.

Submitted By: place the name of the LHD or PHR 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.

Shipping Requirements

Three labels are required on the package to ship serum:

1. Shipping label addressed to National Jewish Health Laboratories
2. Category B Biological Substance label UN3373
3. Dry Ice label UN1845

1. Shipping Label. Address "To":

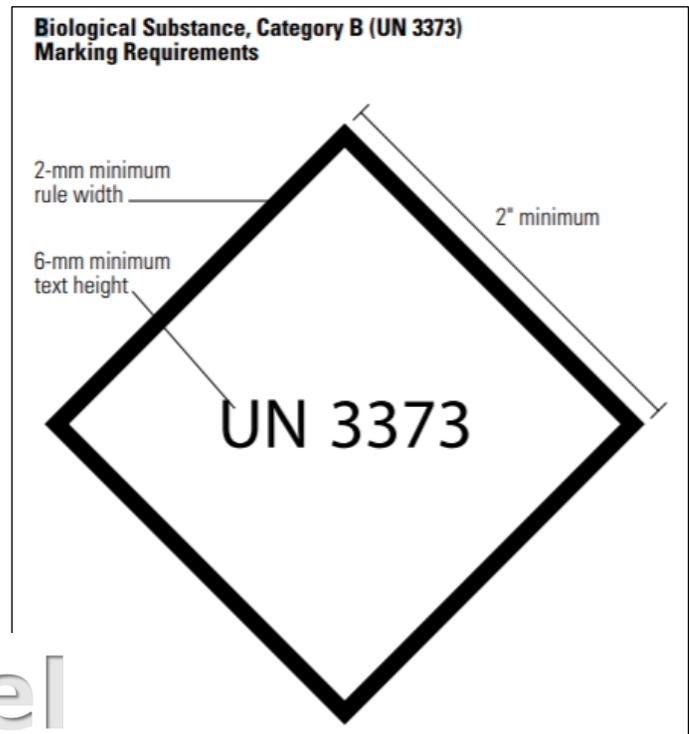
National Jewish Health
Pharmacokinetics Laboratory
1400 Jackson Street, K425
Denver, CO 80206

2. Category B – Biological Substances Label UN3373

From FedEx: "Biological Substance, Category B" must appear in 6-mm-high text on the outer package adjacent to a diamond-shaped mark. The UN 3373 marking must be in the form of a square set at an angle of 45 degrees. Each side of the UN 3373 diamond should measure a minimum of 2" (50 mm). The width of the diamond rule line must be a minimum of 2 mm, and the letters and numbers must be at least 6 mm high."

Contact FedEx for labels, or go to a FedEx location for assistance.

https://www.fedex.com/content/dam/fedex/us-united-states/services/UN3373_fxcom.pdf



Sample label

3. Dry Ice – Class 9 Miscellaneous Dangerous Goods UN1845

An International Air Transport Association (IATA) Class 9 Miscellaneous label must appear on all dry ice shipments. FedEx Express offers a dry ice label that, when correctly completed, satisfies the IATA marking and labeling requirements, available free of charge at fedex.com or by calling 1.800.GoFedEx 1.800.463.3339

The following permanent markings are required on the outer packaging of all IATA dry ice shipments:

- “Dry Ice”
- “UN 1845”
- Net weight of dry ice in kilograms
- Name and address of the shipper
- Name and address of the recipient

Sample label



To print labels, follow this link:

https://www.fedex.com/content/dam/fedex/us-united-states/services/Dry_Ice_Label.pdf

Supplies Needed

Local and regional TB programs may need to purchase additional supplies for collecting and shipping the serum drug levels. Contact the laboratory at National Jewish Health for questions regarding acceptable supplies at 1-800-550-6227.



- Plain red or green 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/green 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 and required for shipping.



- Cold Boxes for Shipping**
If the FedEx cold box is not adequate size for specimen and the three pounds of dry ice needed for shipping, a vaccine-size cold box is recommended.

Additional Resources

National Jewish Laboratory Requisition:

https://www.nationaljewish.org/NJH/media/ADX/Requisitions/ADx700-Pharmacokinetics_Req_10-2018.pdf

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 from National Jewish:

<https://www.nationaljewish.org/for-professionals/diagnostic-testing/adx/diagnostic-testing/shipping-guidelines>

Shipping and Labeling Requirements for Category B shipping from FedEx:

https://www.fedex.com/content/dam/fedex/us-united-states/services/UN3373_fxcom.pdf

DSHS-Recognized Tuberculosis Medical Consultants:

<http://www.dshs.texas.gov/idcu/disease/tb/consultants/>

DSHS TB and Hansen's Disease Branch Third Thursday's Brown Bag, "Therapeutic Drug Monitoring":

<https://www.dshs.state.tx.us/idcu/disease/tb/Calendar/>