Texas Department of State Health Services Standing Delegation Orders for Tuberculosis Clinical Services Provided by Authorized Licensed Nurses, Fiscal Year 2025

The purpose of this document is to provide authority for specific acts of tuberculosis (TB) clinical services described by the TB and Hansen's Disease Unit and under the authority of Rule Title 22, Texas Administrative Code §193.2, Standing Delegation Orders.

Standing delegation orders (SDOs) and standing medical orders (SMOs) are written instructions, orders, rules, regulations or procedures prepared by a physician. SDOs provide authority and a plan for use with patients presenting themselves prior to being examined or evaluated by a physician. SMOs provide authority and direction for the performance of certain prescribed acts for patients which have been examined or evaluated by a physician. SDOs and SMOs are distinct from specific orders written for a particular patient. The Texas TB Manual should be used as a companion to this SDO in order to ensure all patient care standards are met. The intended audience for these orders is authorized licensed nurses working in local health departments providing TB services, and in Texas Department of State Health Services (DSHS) Public Health Regions.

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Standing Delegation Orders

A. Definitions

1. Authorized Licensed Nurse: an employee or contractor of the Texas Department of State Health Services in a nursing position who has met the requirements of and signed this SDO.

2. Authorizing Physician: a physician licensed by the Texas Medical Board who executes this SDO.

3. Licensed Healthcare Provider: a licensed healthcare provider (physician assistant, advanced practice nurse, physician) who is responsible for the care of the patient. The licensed healthcare provider may be another provider who is providing care for the patient in the medical community, or it may be the authorizing physician, if the patient does not have another provider.

B. Method Used for Development, Approval, and Revision

This SDO and the relevant attachments shall be:

1. Developed by the TB and Hansen's Disease Unit.

2. Reviewed, updated, and signed at least annually by the authorizing physician who may re-name these Standing Delegation Orders for local use and write any additional orders, provide clarification or include updates as needed to reflect local practice, with the standards outlined in this document as the minimum orders.

3. Revised as necessary by the DSHS Infectious Diseases Medical Officer, the Regional Medical Directors, and/or the TB and Hansen's Disease Unit.

4. Reviewed (and revised as necessary) annually by Heartland National Tuberculosis Center http://www.heartlandntbc.org/.

C. Level of Experience, Training, Competence, and Education Required

To carry out acts under this SDO, an authorized licensed nurse must:

1. Be an employee or contractor of the Texas DSHS.

2. Be currently licensed to practice by the Texas Board of Nursing.

3. Be currently certified in Basic Life Support.

4. Have reviewed, are familiar with, and able to readily access the

recommendations within the following documents:

a. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clinical Infectious Diseases (2016), 63 (7): e147-e195. https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf
b. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children (2016). Clinical Infectious Diseases (2016), 64 (2):111-115. https://pubmed.ncbi.nlm.nih.gov/28052967/
c. Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020. https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6901a1-H.pdf
d. Testing and Treatment of Latent Tuberculosis Infection in the United States, 3rd Edition, 2023. http://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/
e. Treatment of Drug-Resistant Tuberculosis, An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline (2019). American Journal of Respiratory Critical Care Medicine 15; 200 (10): e93-e142. https://www.atsjournals.org/doi/full/10.1164/rccm.201909-1874ST.
f. Provisional CDC Guidance for the Use of Pretomanid as part of a Regimen (Bedaquiline, Pretomanid, and Linezolid [BPAL]) to Treat Drug-Resistant Tuberculosis Disease. CDC, 2022. https://www.cdc.gov/tb/hcp/treatment/bpal.html?CDC_AAref_Val=https://www.cdc.gov/tb/topic/drtb/bpal/default.htm.
g. Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection. MMWR. 2011; 60(48):1650–1653. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w

    Update of Recommendations for Use of Once-Weekly Isoniazid-Rifapentine Regimen to Treat Latent *Mycobacterium tuberculosis* Infection (2018) https://www.cdc.gov/mmwr/volumes/67/wr/mm6725a5.htm?s_cid=mm6725a5_w
h. The Spectrum of Tuberculosis from Infection to Disease-TB at a Glance: 3rd Edition. Heartland National TB Center and Mayo Clinic, 2020. https://www.heartlandntbc.org/wp-

content/uploads/2021/12/The_Spectrum_of_TB.pdf

i. American Academy of Pediatrics (AAP). Red Book: 2024 – 2027. Report of the Committee on Infectious Diseases, 33rd edition. https://publications.aap.org/redbook/book/755/Red-Book-2024-2027-Report-of-the-Committee-on.

j. Tuberculosis Risk Factors. CDC, 2024. https://www.cdc.gov/tb/risk-factors/?CDC_AAref_Val=https://www.cdc.gov/tb/topic/testing/whobetested.htm

k. Screening and Testing for HIV, Viral Hepatitis, STD & Tuberculosis in Pregnancy. CDC, 2024. https://www.cdc.gov/pregnancy-hiv-std-tb-hepatitis/php/screening/

l. AIDSInfo Clinical Guidelines Portal. https://clinicalinfo.hiv.gov/en

m. Core Curriculum on Tuberculosis: What the Clinician Should Know, 7th Edition. CDC, 2021. https://www.cdc.gov/tb/hcp/education/core-curriculum-on-tuberculosis.html?CDC_AAref_Val=https://www.cdc.gov/tb/education/corecurr/index.htm

n. Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection — United States, 2010. MMWR. 2010; 59(5):1-25. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5905a1.htm?s_cid=rr5905a1_e

o. Consensus statement on the use of Cepheid Xpert MTB/RIF assay in making decision to discontinue airborne infection isolation in healthcare settings. National Tuberculosis Controllers Association (NTCA) and Association of Public Health Laboratories (APHL), April 2016. http://www.tbcontrollers.org/docs/resources/NTCA_APHL_GeneXpert_Consensus_Statement_Final.pdf.

p. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health Care Settings. MMWR. 2006; 55(RR14):1-17. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm

q. An Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy. Am J Respir Crit Care Med. 2006; 174:935-952. http://www.thoracic.org/statements/resources/mtpi/hepatotoxicity-of-antituberculosis-therapy.pdf

r. Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings, 2005. MMWR 2005; 54(RR17):1-141. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm?s_cid=rr5417a1_e

Update: Tuberculosis Screening, Testing, and Treatment of U.S. Health Care Personnel: Recommendations from the National Tuberculosis

Controllers Association and CDC, 2019. MMWR. May 17, 2019 / 68(19);439–443 https://www.cdc.gov/mmwr/volumes/68/wr/mm6819a3.htm?s_cid=mm6819a3_w

s. Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis. MMWR 2005; 54(RR15): 1-55. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm
t. Controlling Tuberculosis in the United States Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. MMWR. 2005; 54(RR12):1-81. http://www.cdc.gov/MMWR/preview/MMWRhtml/rr5412a1.htm
u. Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection. MMWR. 2000; 49(RR06):1-54. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm
   Update: Adverse Event Data and Revised American Thoracic Society/CDC Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection – United States, 2003. MMWR. 2003; 52(31):735-739. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5231a4.htm
v. Recommendations for Prevention and Control of Tuberculosis among Foreign-Born Persons. MMWR. 1998; 47(RR16):1-26. http://www.cdc.gov/MMWR/preview/MMWRhtml/00054855.htm
w. Tuberculosis Control Laws-United States, 1993 Recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR.1993;42(RR15). http://www.cdc.gov/mmwr/preview/mmwrhtml/00030715.htm
x. Prevention and Control of Tuberculosis in Migrant Farm Workers Recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR. 1992; 41(RR10). http://www.cdc.gov/MMWR/preview/MMWRhtml/00032773.htm
y. Prevention and Control of Tuberculosis Among Homeless Persons Recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR. 1992; 41(RR5):001. http://www.cdc.gov/MMWR/preview/MMWRhtml/00019922.htm

5. Have undergone an initial or continuing evaluation of competence relevant to TB clinical services within 12 months prior to signing and providing TB clinical services under this SDO:
   a. Initial evaluation of competence is performed by the authorizing physician, the nurse's supervisor, or clinical designee and consists of completion of 40 hours of continuing education and skills training (including the CDC's "Self-Study Modules on Tuberculosis"

https://www.cdc.gov/tb/hcp/education/self-study-modules-on-tuberculosis.html) as approved by the local or regional TB program manager, and completion of a mentoring plan facilitated by an experienced TB nurse and/or licensed healthcare provider.

1) The authorized licensed nurse must receive an initial evaluation by the authorizing physician, the nurse's supervisor, or clinical designee that documents the nurse's ability to carry out these orders in the customary manner.
2) For authorized licensed nurses whose primary job duties are with the TB program, this training and evaluation of competence must occur within 90 days of employment. For other authorized licensed nurses, this training and evaluation of competence must occur before TB clinical services are independently provided by the nurse.

b. Continuing evaluation of competence is performed annually by the authorizing physician, the nurse's supervisor, or clinical designee and consists of completion of 16 hours of continuing education and skills training, as approved by the regional or local TB program manager.
   1) The authorized licensed nurse must receive an annual evaluation by the authorizing physician, the nurse's supervisor, or clinical designee that documents the nurse's ability to carry out these orders in the customary manner.

6. Have reviewed and signed this SDO, **ATTACHMENT 1: *Attestation of Authorized Licensed Nurse,*** within 12 months prior to providing services under this SDO.

D. Method of Maintaining a Written Record of Authorized Licensed Nurses

A record of the authorized licensed nurses who complete the required training and demonstrate competence shall be documented and maintained by the nurse's supervisor in the Local Health Department or Public Health Region office.

E. Authorized Delegated Acts

Authorized licensed nurses may evaluate and provide TB clinical services under this SDO to patients who are undergoing evaluation for TB disease or TB infection or are a contact to a confirmed or suspected TB disease case.

It is the intent of all parties that the acts performed under this SDO shall be in compliance with the Texas Medical Practice Act, the Texas Nursing Practice Act, the Texas Pharmacy Act, and the rules promulgated under those Acts.

F. Procedures and Requirements to be Followed by Authorized Licensed Nurses

1. Adhere to all Standard Precautions, including bloodborne and respiratory precautions, when participating in TB clinical services.

2. Utilize interpreter services to facilitate patient and provider communication as it relates to limited English proficient (LEP) patients. DSHS employees may use the service listed on the following website: https://online.dshs.texas.gov/services/translation-interpretation

3. Establish that the patient requires evaluation for TB disease or TB infection or is a contact to a confirmed or suspected TB disease case.

4. Ensure, to the extent possible, that the patient seen for TB clinical services is, in fact, who the person claims to be.

5. Ensure the patient's consent, in the preferred language of the patient, and signature have been obtained in accordance with agency policy and provide copies of the ***DSHS Privacy Notice*** and/or applicable signed consent forms.
   a. ***DSHS General Consent and Disclosure*** (L-36), available at: www.dshs.state.tx.us/rls/pubs/GeneralConsentForm042010.pdf
   b. ***DSHS Privacy Notice***, available at: http://www.dshs.state.tx.us/hipaa/privacynotices.shtm

6. All patients undergoing evaluation for TB disease or TB infection will receive an initial evaluation to consist of:
   a. A personal and medical history.
   b. An appropriate physical examination.
   c. An explanation of all test(s) to be performed and the risk and benefits of each one. Provide the opportunity for the patient to ask questions.
   d. The medical screening as described in **ATTACHMENT 2: *Medical Screening.***
   e. **TB screening tests:** Determine if the patient has had a previous positive TB screening test performed in the United States and if there is written documentation of the results OR if the patient has had previous TB disease and if there is written documentation of the treatment.
      1) If not, perform a TB screening test with an interferon gamma release assay (IGRA), either T-SPOT®.TB test or QuantiFERON®–TB Gold Plus, as determined by the licensed healthcare provider; the tuberculin skin test (TST) may be used if patient is unable to receive an IGRA or refuses phlebotomy, as described in ***ATTACHMENT 3: TB Screening***

Tests, if the patient has no contraindications for the selected TB screening test.

2) If so, do not administer another TB screening test, unless instructed by the licensed healthcare provider. Obtain a copy of the results or treatment and document in the patient's medical record. If the patient has had any past treatment for TB infection, obtain a copy of the treatment, if able, and document in the patient's medical record.

7. Obtain additional diagnostic tests appropriate to the services provided.
   a. **Laboratory Tests:** Determine the need for lab specimen collection, as described in **ATTACHMENT 4: *Laboratory Tests (Labs).*** Determine if the patient has had the appropriate lab specimens collected within the last 14 days and if there is written documentation of the results.
      1) If not, perform venipuncture and collect specimens in the proper tubes, according to laboratory submission requirements.
      2) If so, do not perform venipuncture or collect specimens, unless instructed by the licensed healthcare provider. Obtain a copy of the results and document in the patient's medical record.
   b. **Chest X-Ray:** Determine the need for a CXR, as described in **ATTACHMENT 5: *Chest X-Ray (CXR).*** Determine if the patient has had the appropriate CXR performed within the allowed time frame and if there is written documentation of the results.
      1) If not, refer for and obtain CXR within 14 calendar days if the patient has no contraindications for CXR. TB programs with on-site radiograph equipment should obtain a CXR within ten (10) calendar days.
      2) If so, do not obtain another CXR, unless instructed by the licensed healthcare provider. Obtain a copy of results (and images, if available, for provider review) and document in the patient's medical record.
   c. **Sputum Collection:** Determine the need for sputum collection, as described in **ATTACHMENT 6: *Sputum Collection.*** Determine if the patient has had the appropriate sputum collection(s) performed within the allowed time frame and if there is written documentation of the results.
      1) If not, collect sputum specimens, according to laboratory submission requirements. Otherwise, contact the licensed healthcare provider for instructions.
      2) If so, do not collect sputum, unless instructed by the licensed healthcare provider or unless specimen have gone to a commercial laboratory and obtaining test results is delayed. Obtain a copy of the results and document in the patient's medical record.

8. Label and correctly package specimens, according to shipping requirements

and regional or local procedures. Submit specimens to an approved laboratory for processing.

9. Document the following in the patient's medical record:
   a. All test collection dates, test types, circumstances affecting collection, and results.
   b. That all diagnostic test results were reviewed.

10. For patients suspected or confirmed to have TB disease, provide the Order to Implement and Carry Out Measures for a Patient with Tuberculosis ("Control Order" or the TB 410 or equivalent https://www.dshs.texas.gov/sites/default/files/IDCU/disease/tb/forms/DOCS/TB-410.doc) signed and dated by the local health authority, for the patient to review at the beginning of treatment, if not provided already.
    a. Explain the Control Order and risks of violation of the Control Order. Provide the opportunity for the patient to ask questions. Have the patient review and sign the Control Order.
    b. Provide a copy of the Control Order to the patient.
       1) If the patient has questions the nurse cannot answer, contact the local health authority.
       2) If the patient refuses to sign the Control Order, sign and date that the Control Order was given, and that the patient refused to sign it; this serves as documentation in the event the patient violates the order.
       3) If the patient violates the Control Order, immediately notify the licensed healthcare provider treating the patient and the local health authority who signed the control order.

11. For patients suspected or confirmed to have drug susceptible TB disease, implement location-appropriate isolation (home-based or refer to a negative pressure air-borne infection isolation room [AIIR] if in a congregate setting).
    a. If the patient has an AFB smear positive specimen, do NOT release from isolation until:
       1) The patient has three consecutive negative AFB sputum smears, collected in 8- to 24- hour intervals; and
          - has symptomatic improvement; and
          - has been on multi-drug therapy for tuberculosis **for at least the equivalent of two weeks** given as directly observed therapy (DOT); and
          - has been completely adherent with DOT

       Once the above criteria are met, the patient may be released from isolation, with the date documented in the medical record.

b. If the patient has <u>never</u> had an AFB smear positive sputum or other respiratory specimen, do NOT release from isolation until:

1) The patient has three consecutive negative AFB sputum smears, collected in 8- to 24- hour intervals; <u>and</u>
2) has symptomatic improvement; and
3) has been on multi-drug therapy for tuberculosis for **at least 5 days** given as directly observed therapy (DOT); and
4) Has been completely adherent with DOT.

Once the above criteria are met, the patient may be released from isolation with the date documented in the medical record.

c. If the patient has positive AFB sputum smears and the last two consecutive sputum specimens return AFB culture negative, they may be released from isolation if they meet the following criteria (*even if they remain smear positive, as these likely represent dead organisms)*:

1) have symptomatic improvement; and
2) have been adherent with multi-drug therapy for tuberculosis given as directly observed therapy (DOT).

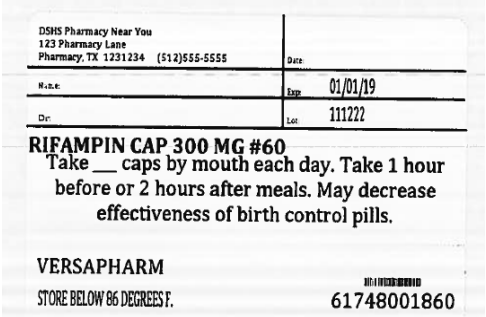
12. Before medications are administered or provided to the patient, send all pertinent clinical information to the licensed healthcare provider for review. Ensure there is a current order for medication and include when medications are held and need to be restarted.
    For verbal or telephone orders, or for telephonic reporting of critical test results, verify the complete order or test result by recording the complete order or test result in the patient's medical record and "reading-back" the complete order or test result. Receive confirmation from the licensed healthcare provider who gave the order or received the test result.
    All verbal or telephone orders should be reviewed and countersigned or confirmed by written communication as soon as possible, ideally within one week.

13. The authorized licensed nurse shall review the most recent TB medication regimen ordered by the licensed healthcare provider, a copy of which is placed in the medical record, ensuring that an updated medication consent form is updated in the chart as needed.
    a. Verify appropriate weight-based dosage calculations for all patients. For purposes of dosage calculations and treatment regimen selection, a patient is considered a child if the patient is less than 18 years old and should receive pediatric weight-based dosing of medications as described in **ATTACHMENT 7: *Medications.***

14. Determine whether the patient is taking medications that interact when used with the prescribed TB medication regimen. Seek out/consult with a trusted drug information source (e.g., DSHS Library access to "Facts and Comparison," DSHS pharmacist, prescribing licensed healthcare provider) to verify possible medication interactions.
    a. If so, do not administer or provide medications. Notify the licensed healthcare provider for instructions.
    b. If not, administer (for directly observed therapy [DOT]) or provide (for self-administered therapy) medications consistent with the most recent licensed healthcare provider order.
        1) If medications are to be administered by **DOT**, verify the medications administered are the same as the medications ordered, provide the DOT packet(s) to the patient, and observe the patient ingesting all prescribed medication in each DOT dose packet.
        2) If medication(s) are to be **self-administered** by the patient, complete the medication label and provide the medication(s) to the patient.
            i. As required by the Texas State Board of Pharmacy (Rule Title 22, Texas Administrative Code §291.93), the following information will be pre-printed on the medication label for self-administered medications:
                - The name, address, and telephone number of the clinic
                - The name and strength of the drug - if generic name, the name of the manufacturer or distributor of the drug
                - Quantity, Lot number, Expiration date

            ii. The authorized licensed nurse will complete the labeling directions so that it contains the following information:
                - The patient's name
                - Date medication is provided
                - The physician's name
                - Directions for use (per Texas State Board of Pharmacy rules, incomplete directions for use may be present and if so, are to be completed by the authorized licensed nurse at time of provision).

    See sample label:



3) Counsel the patient regarding possible side-effects, conditions under which medications should be stopped and the clinic contacted, and the need to prevent pregnancy, if applicable.
4) Provide patient with a Patient Education Sheet outlining the uses of the drug(s), potential side effects, and other precautions.
5) Document on Medication Provision Log patient's name or initials, drug(s) given (name, strength, quantity), and initials of nurse providing the medications.
6) The initial dose of each new TB medication should be given by an authorized licensed nurse with emergency supplies readily available, when possible. The patient should remain for 30 minutes for observation of adverse reactions. Document how long the patient was observed.

15. The following ***must* be provided via DOT** until completion of therapy:
    a. All regimens for TB disease
    b. Intermittent regimens for TB infection (self-administration may be considered on select patients for 3HP; see **ATTACHMENT 7: *Medications***).
    c. All treatment for TB infection for contacts to multi-drug resistant (MDR)-TB, pre-extensively drug-resistant (pre-XDR) TB, or extensively-drug resistant (XDR)-TB

16. The following is **highly recommended to be provided via DOT** until completion of therapy:
    a. Children less than 5 years old on treatment for TB infection (including window prophylaxis).

17. If any of the following is true, contact the licensed healthcare provider. Do not initiate treatment until additional orders are given.
    a. The medication prescribed for TB disease or TB infection is not consistent with recommended regimens as described in **ATTACHMENT 7: *Medications***.
    b. The medication prescribed for a patient co-infected with TB disease and HIV infection is ordered to be given twice weekly.
    c. The medication prescribed for TB disease or TB infection is not appropriate for the patient's weight and/or age as described in **ATTACHMENT 7: *Medications***.
    d. Medication prescribed for TB disease or TB infection is not consistent with:
        1) Available and known drug susceptibilities for TB disease
        2) Consult recommendations provided by a DSHS-recognized TB Medical Consultant

e. Contraindications or significant drug interactions exist with non-TB medications the patient is currently taking, and the TB medication prescribed.
f. Patient is suspected or known to be pregnant.
g. Patient has active hepatitis or end stage liver disease.
h. Laboratory test results are not within the normal range.
i. Patient meets indications for DOT but has been prescribed self-administered medications. Consultation with the authorizing physician must be obtained. An order or progress note in writing from the licensed healthcare provider must be placed in the patient's medical record stating reasons for not providing medications by DOT, as expected by DSHS.

18. Immediately hold treatment and contact the licensed healthcare provider if any of the following occurs. Obtain testing as described in **ATTACHMENT 4: *Laboratory Tests*** and consult the licensed healthcare provider before restarting any medications.
    a. Aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT), level exceeds three times the upper limit of normal in the presence of symptoms.
    b. AST and/or ALT level exceeds five times the upper limit of normal (with or without symptoms).
    c. Bilirubin exceeds two times the upper limit of normal.
    d. Laboratory monitoring results reveal a significant change, *as defined by the licensed healthcare provider,* in white blood cell count, hemoglobin, or platelet count.
    e. Patient reports symptoms or has signs that could be attributed to medication toxicity.
    f. Patient is on treatment for TB infection and develops signs or symptoms of TB disease.

19. Notify the licensed healthcare provider for any interruptions of therapy, as defined in **ATTACHMENT 7: *Medications.***
    a. Interruptions in treatment may have a significant effect on the duration of therapy. Reinstitution of treatment must take into account the bacillary load of the patient, the point in time when the interruption occurred, and the duration of the interruption.
    b. In general, the earlier in treatment and the longer the duration of the interruption, the more serious the effect and the greater the need to restart therapy from the beginning.

20. **Determine completion of therapy based on total number of doses administered** (allowing for minor interruptions in therapy) - *not on duration*

of therapy alone - as described in **ATTACHMENT 7: *Medications*.** Every attempt should be made to help patient ***not*** miss doses. Completion of treatment for initial phase must be documented before the patient is permitted to begin therapy for continuation phase of treatment for TB disease. **Only after the minimum total number of DOT doses has been administered for the initial phase can DOT doses be counted towards the minimum total number of doses administered for the continuation phase.** Drug susceptibility testing should be known before discontinuing medications in the initial and continuation phases.

21. If the authorized licensed nurse has questions or concerns that the licensed healthcare provider is unable to answer, the question or concern should be referred to the regional TB program manager and/or the Regional Medical Director, when applicable. The DSHS TB and Hansen's Disease Unit may also be consulted for further information and direction.

22. If any of the conditions are met in **ATTACHMENT 9: *DSHS-Recognized TB Medical Consultant Indications***, a DSHS-Recognized TB Medical Consultant should be consulted. See http://www.dshs.texas.gov/idcu/disease/tb/consultants/.
    a. Exceptions may be granted if made by the DSHS Regional Medical Director (RMD). In that case, the RMD must either write the medical orders for the patient or include a signed letter in the patient's medical record that the treatment prescribed meets criteria for adequate therapy. The RMD may also request a consult from a DSHS-Recognized TB Medical Consultant.
    b. All consults should include the specific question to be answered, adequate information regarding the history, physical, and diagnostic test results, and a cc: to the regional TB Program Manager, the Regional Medical Director, and the TB and Hansen's Disease Unit Nurse Consultant(s).

G. Patient Record-Keeping Requirements

TB forms available at: https://www.dshs.texas.gov/disease/tb/forms.shtm. Authorized licensed nurses must accurately and completely report and document each patient visit in a medical record prepared in accordance with local and DSHS policy or regional procedures, which will include:

1. Names of personnel involved in the evaluation and treatment at each visit, including the name of the interpreter (if an interpreter is used).

2. The patient's personal health history, the patient's status including signs and symptoms, and physical examination findings.

3. Actions carried out under these standing orders.

4. Any additional physician orders.

5. Medications administered, prescribed by the physician, or provided to the patient.

6. Patient response(s), if any.

7. Contacts with other healthcare team members (e.g., the patient's primary healthcare provider) concerning significant events regarding patient's status.

8. Documentation that the appropriate forms are completed and included in the medical record, and copies, when applicable, are provided to the patient.

H. Scope of Supervision Required

These Standing Delegation Orders give the authorized licensed nurse authority to perform the acts described in the SDOs in consultation with the authorizing physician as needed.

I. Specialized Circumstances to Immediately Communicate with the Authorizing Physician

Specific circumstances that the authorized licensed nurse providing services under this SDO should immediately contact the authorizing physician by phone include, but are not limited to:

1. Circumstances when medical direction or consultation is needed.

2. Patient has violated the signed *Order to Implement and Carry Out Measures for a Patient with Tuberculosis.*

In an emergency situation, the authorized licensed nurse is to call 911, provide emergency services as authorized in the regional or local emergency SDO, and contact his/her supervisor and/or the authorizing physician by phone as soon as possible.

J. Limitations on Setting

Authorized licensed nurses can provide services under these standing orders in the clinic setting, in the patient's home, or other field settings when the authorizing physician can be contacted by phone.

K. Date and Signature of the Authorizing Physician

This SDO shall become effective on the date that it is signed by the authorizing physician, below, and will remain in effect until it is either rescinded, upon a change in the authorizing physician, or at the end of business on the last day of the current DSHS fiscal year (August 31, 2025), whichever is earlier.

Authorizing Physician's Signature:

_____

Authorizing Physician's Title:

_____

Printed Name:

_____

Effective Date:

_____

Emergency Contact Information:

_____

ATTACHMENT 1: Attestation of Authorized Licensed Nurse

I, _____ have read and understand the
printed name of authorized licensed nurse

Texas Department of State Health Services Standing Delegation Orders for Tuberculosis Clinical Services Provided by Authorized Licensed Nurses, Fiscal Year 2025 ("SDO") that was signed by Dr._____
printed name of authorizing physician
on_____.
date of authorizing physician's signature

- I agree that I meet all qualifications for authorized licensed nurses outlined in the SDO.
- I agree to follow all instructions outlined in the SDO.

Signature of Authorized Licensed Nurse Date

ATTACHMENT 2: Medical Screening

A. <u>All patients undergoing initial screening for TB disease or TB infection:</u>

1. Undergo a **clinical evaluation** that includes a signs and symptoms screening questionnaire and documentation of medical history.

2. **Screen for tuberculosis** with an approved TB screening test, as outlined in Attachment 3: *TB Screening Tests*. Perform venipuncture and collect specimens in the proper tubes, according to laboratory submission requirements.

3. **Screen for HIV infection** per the following:
   a. For patients aged 12 and older, screen using an approved laboratory-based HIV immunoassay.
   b. For patients younger than 12 years old, screen for HIV infection using an approved laboratory-based HIV immunoassay **if risk factors for HIV infection are present** (refer to: https://www.cdc.gov/healthyyouth/about/dash-snapshot.htm; http://www.pedaids.org/pages/about-pediatric-aids):
      1) known or self-reporting of mother with HIV infection and no documentation of child's status;
      2) history of blood transfusion outside the U.S.;
      3) history of sexually transmitted infection (STI);
      4) sexual activity;
      5) pregnancy; and/or
      6) intravenous drug abuse.
   c. For patients screened (as per risk factors above) aged <24 months:
      1) HIV infection in infants should be diagnosed using HIV nucleic acid amplification virologic assays. (refer to: https://clinicalinfo.hiv.gov/en/guidelines/perinatal/diagnosis-hiv-infection-infants-and-children?view=full).
      2) Because children with perinatal HIV exposure aged 18 to 24 months may have residual maternal HIV antibodies, definitive exclusion or confirmation of HIV infection in children in this age group who are HIV antibody-positive should be based on a nucleic acid test (refer to: https://clinicalinfo.hiv.gov/en/guidelines/perinatal/diagnosis-hiv-infection-infants-and-children).
      3) DSHS laboratory does not perform HIV NAAT testing but can provide guidance where to send the specimen if needed; contact DSHS serology lab for details: http://www.dshs.texas.gov/lab/default.shtm.

If any of the following apply, **do not screen for HIV**:

a. If the patient has a previously documented positive HIV test result, HIV

testing does not need to be repeated. Obtain a copy of the results and document in the patient's medical record.

b. If the patient has a documented negative HIV test result from a specimen collected within the last 14 days, HIV testing does not need to be repeated. Obtain a copy of the results and document in the patient's medical record.

B. <u>All patients undergoing evaluation for TB disease or TB infection, once initially screened, and diagnosed:</u>

1. For patients aged 12 years or older, **screen for diabetes** per the following:
    a. For patients with suspected or known diabetes, screen using a fasting blood glucose.
    b. For non-diabetic patients, screen using a random blood glucose.

    If any of the following apply, **do not screen for diabetes**:
    a. If the patient is younger than 12 years old, routine screening is not recommended.
    b. If the patient has the appropriate documented diabetes test result from a specimen collected within the last 14 days, diabetes testing does not need to be repeated. Obtain a copy of the results and document in the patient's medical record.

2. For patients with any of the following risk factors for hepatitis B virus (HBV), **screen for HBV** using hepatitis B surface antigen (HBsAg):
    a. All persons born in one of the following high-risk regions:
        1) Western Pacific (includes China, Cambodia, Vietnam, the Philippines, Korea)
        2) Africa (Democratic Republic of Congo, Ethiopia, Guinea, Kenya, Eritrea, Sierra Leone)
        3) Southeast Asia (Bangladesh, Nepal, India, Myanmar/Burma)
        4) Eastern Mediterranean (Afghanistan, Iraq, Kuwait, Pakistan, Yemen, Sudan, Syria)
        5) Additional information can be found at: https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/hepatitis-b
    b. U.S. born persons not vaccinated as infants
    c. Persons with behavioral exposures to HBV (e.g., men who have sex with men, past or current injection drug users, history of incarceration)
    d. Persons with liver disease or elevated ALT/AST of unknown etiology
    e. Pregnant women
    f. Household contacts and sex partners of HBV-infected persons
    g. Persons with HIV

If any of the following apply, **do not screen for HBV**:

a. If the patient has a previously documented positive HBV test result, HBV testing does not need to be repeated. Obtain a copy of the results and document in the patient's medical record.
b. If the patient has a documented negative HBV test result from a specimen collected within the last 14 days, HBV testing does not need to be repeated. Obtain a copy of the results and document in the patient's medical record.

3. For patients born during 1945 through 1965 (without prior ascertainment of hepatitis C virus (HCV) risk factors) or for patients with any of the following risk factors for HCV infection, **screen for HCV** using an FDA-cleared test for antibody to HCV (i.e., immunoassay, enzyme immunoassay (EIA)or enhanced chemiluminescence immunoassay (CIA) and, if recommended, a supplemental HCV test):
    a. Current or past injection drug use, including those who injected once or a few times many years ago
    b. History of incarceration
    c. Have certain medical conditions, including persons:
        1) Who received clotting factor concentrates produced before 1987
        2) Who were ever on long-term hemodialysis
        3) With persistently abnormal ALT levels (if known/previously documented)
        4) Who have HIV infection
    d. Were prior recipients of transfusions or organ transplants, including persons who:
        1) Were notified that they received blood from a donor who later tested positive for HCV infection
        2) Received a transfusion of blood, blood components or an organ transplant before July 1992
    e. Being born to a mother with HCV infection
    f. Intranasal drug use
    g. Receipt of an unregulated tattoo
    h. Other percutaneous exposures

If any of the following apply, **do not screen for HCV**:

a. If the patient has a previously documented positive HCV test result, HCV testing does not need to be repeated. Obtain a copy of the results and document in the patient's medical record.
b. If the patient has a documented negative HCV test result from a specimen collected within the last 14 days, HCV testing does not need to

be repeated. Obtain a copy of the results and document in the patient's medical record.

Additional information can be found at: https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/hepatitis-c

4. Ask the patient about his or her vaccination history. Obtain documentation and confirm in ImmTrac. If the patient's vaccination status is not current, determine if the patient meets current DSHS or local Immunization Program eligibility criteria.
   a. If so, immunization may be provided as authorized in the appropriate immunization SDO. Note the issue regarding administering live virus vaccines and the timing of TB screening tests in Attachment 3.
   b. If not, refer patient to an appropriate immunization provider resource for vaccination.

C. ***Patients suspected or confirmed to have drug susceptible TB disease and who are prescribed treatment*** will have the following medical screening(s):

1. **Baseline and monthly clinical monitoring** and evaluation for TB medication toxicity:
   a. If patient is taking **ethambutol**, this includes red/green color discrimination using Ishihara plates and visual acuity using Snellen chart.
   b. If patient is taking **rifabutin**, this includes asking about eye pain, overall vision changes, and/or sensitivity to light.
   c. If patient is taking **high dose isoniazid**, this is to include screening for peripheral neuropathy.

2. **Clinical evaluation as soon as feasible** when signs or symptoms of medication toxicity develop. In this case, hold the medications, contact the licensed healthcare provider, do not resume until re-started by the provider.

D. ***Patients receiving treatment for TB infection (including patients on window prophylaxis)*** will have the following medical screening(s):

1. **Baseline and monthly clinical monitoring** and evaluation for TB medication toxicity.
   a. If patient is taking **rifabutin**, this includes asking about eye pain, overall vision changes, and/or sensitivity to light.

2. **Clinical evaluation as soon as feasible** when signs or symptoms of medication toxicity develop. In this case, hold the medications, contact the licensed healthcare provider, do not resume until re-started by the provider.

ATTACHMENT 3: TB Screening Tests

A. *<u>The following patients may undergo TB screening testing:</u>*

1. All patients undergoing evaluation for, or diagnosed with, TB disease and there is not a documented previous positive tuberculin skin test (TST), or interferon-gamma release assay (IGRA) result performed in the United States or documented previous TB disease, *unless the criteria in #6 apply.*

2. All patients undergoing evaluation for TB infection and there is not a documented previous positive TST or IGRA result performed in the United States *unless the criteria in #6 apply.* Patients with history of severe reaction to a TST (i.e., blistering) should not have a repeat TST.

3. All contacts who meet criteria for testing, and there is not a documented previous positive TST or IGRA result or documented previous TB disease.
   a. If the initial TB screening test is negative, administer a second TB screening test 8 to 10 weeks after the last exposure.
   b. See **ATTACHMENT 7: *Medications*** for indications for window prophylaxis and recommendations to complete a full course of treatment for TB infection (beyond the window period) even if a TB screening test administered 8 weeks or more after the end of exposure is negative.

4. All patients who meet criteria for targeted testing, except screening in correctional facilities – monthly screening reports shall be submitted in accordance with TB and Hansen's Disease Unit.

5. DSHS employees and contractors providing TB services, when TB screening is indicated.

6. Class B immigrants or other immigrants* (including refugees) undergoing immigration screening.
   a. **Exceptions**: Immigrants who need evaluation for TB, including those who are reported from the Electronic Disease Notification (EDN) system with a classification of A or B, will have the following exceptions to <u>repeat</u> testing:
      1) Applicants with a documented positive IGRA test, even if performed overseas, do not need to have a repeat IGRA at the health department unless indicated by the licensed healthcare provider.

      Note: For all applicants, an IGRA is strongly preferred if the last test overseas was a positive TST only. Consideration of diagnosis should be

made based on the IGRA result; however, the licensed healthcare provider will need to consider items listed in B. 4., below.

Applicants referred from a civil surgeon should <u>not</u> undergo a TB screening test initially at the health department; they should be referred to the health department <u>only</u> after a full evaluation has been done by the civil surgeon (that includes IGRA/TST and CXR).

Refer to: https://www.cdc.gov/immigrant-refugee-health/hcp/civil-surgeons/tuberculosis.html.

B. <u>TB screening tests may include TST OR IGRA:</u>

1. It is important before applying a TB screening test that information is known about the patient's risk for infection and risk for progression to disease if infected. The single test that is most appropriate for the patient should be chosen and applied. More than one test should not be routinely performed.

2. Routine testing with BOTH a TST and an IGRA is not recommended. If an IGRA is chosen, it should be used in place of, NOT IN ADDITION TO, a TST.

3. Performing both a TST and an IGRA can be considered in the following situations after consulting with the licensed healthcare provider and receiving a patient-specific order for the additional test:
    a. The initial test is negative and the risk for infection, the risk for progression, and the risk for a poor outcome are increased (e.g., when persons with HIV infection or children aged younger than five years are at increased risk for *Mycobacterium tuberculosis* (*M.tb*) infection), or
    b. The initial test is negative and clinical suspicion exists for active tuberculosis disease (such as in persons with symptoms, signs, and/or radiographic evidence suggestive of active tuberculosis disease) and confirmation of *M.tb* infection is desired.
    c. The initial test is positive and additional evidence of infection is required to encourage compliance or to confirm the positive test (e.g., in foreign-born health-care workers who believe their positive TST result is attributable to BCG). A positive IGRA might prompt greater acceptance of treatment for latent TB infection (LTBI) as compared with a positive TST alone.
    d. The initial test is positive, and the patient is considered a healthy person who has a low risk for both infection and progression.
4. If both an IGRA and a TST are performed and discordant results are obtained, the licensed healthcare provider will need to decide regarding whether or not the patient should be considered to have TB infection, based on patient's risk

factors, examination, and epidemiology (such as exposure risk). The TB and Hansen's Disease Unit can assist but cannot make this determination in lieu of the licensed healthcare provider.

5. If both an IGRA and a TST are performed because the initial test is negative, a positive result from a second test increases detection sensitivity. If the repeat test is positive and the patient is high risk, any positive test result should be considered evidence of TB infection and acted upon accordingly. If the second test is negative and the patient is high risk, it still does not conclusively rule out *M.tb* infection. Multiple negative results from any combination of these tests cannot exclude *M.tb* infection.

6. If both an IGRA and a TST are performed because the initial test is positive, a positive result from the second test increases the likelihood that the test result reflects infection.
    a. An alternative is to assume, *without additional testing,* that the initial result is a false positive or that the risk for disease does not warrant additional evaluation or treatment, regardless of test results. This should only be considered after careful assessment of the patient's risk, physical exam findings and history of exposure.
    b. Steps should be taken to minimize unnecessary and misleading testing of persons at low risk.

7. Repeating an IGRA or performing a TST should be considered when the initial IGRA result is indeterminate, borderline, invalid, or if interpretation results are in question and a reason for testing persists.
    a. If an IGRA is to be repeated, a new blood sample should be used. In such situations, repeat testing with another blood sample usually provides interpretable results.

8. A TST is not recommended to be repeated unless the administration or reading of the TST is determined to be unreliable, the tuberculin PPD is determined to be expired, or if performed as 2nd round screening 8-10 weeks after a break in exposure.

9. When screening for TB with a TST or IGRA in persons who have been recently vaccinated, additional factors should be considered.
    a. Live virus vaccines may impact TST or IGRA results due to temporary immune suppression, potentially causing false-negative reactions.
        1) Live virus vaccines include measles, mumps, rubella, varicella, zoster, yellow fever, intranasal influenza, oral polio and smallpox

2) The CDC has issued national guidance on the timing of IGRAs, TSTs, and COVID-19 vaccinations. As this guidance may change when new vaccines and data are available, refer to the NTCA COVID-19 website for current guidance: http://www.tbcontrollers.org/resources/tb-and-covid-19.

b. When possible, placing a TST or drawing an IGRA should occur prior to vaccinations.
c. When that is not possible, a TST or IGRA should not be delayed in persons with risk factors for TB. Providers may order a repeat screening test 4 weeks after vaccination if the initial test is negative.
d. Contact the licensed healthcare provider before making decisions to delay a TST or IGRA for at-risk persons.
e. Vaccinations should not be delayed accommodating TB screening procedures, as a repeat screening may be arranged as needed.

C. ***Which TB screening test to choose:***

1. Before a TB screening test is performed, the advantages and limitations of TST and IGRA must be evaluated for each patient.
    a. Per the American Academy of Pediatrics (AAP) Redbook, 2024, 33rd Edition: "Either TST or IGRA testing is acceptable for children of any age."

2. An IGRA is *preferred* for testing the following groups or individuals:
    a. High-risk individuals who have previously received BCG
    b. Congregate settings, for employees and residents
    c. Persons with diabetes or on dialysis
    d. Immunocompromised persons
    e. Persons undergoing contact investigation
    f. Persons who work with TB patients
    g. Persons anticipated to receive TNF-α inhibitors or other biologic response modifiers

3. If an IGRA is used, there is no preference for the use of one IGRA over another.

4. When IGRA testing is performed greater than 3 days after TST, the PPD injection should be expected to boost anamnestic immune responses measured by IGRA originating from *M.tb* infection (but not from BCG vaccination or in non-sensitized persons). The effect also appears to be more apparent in those individuals who are already IGRA positive. To date, there is no definitive data, and some experts suggest waiting 3 months after TST

before testing with IGRA, while others feel this is unnecessary. **Decisions to delay IGRA testing can only be made by the licensed healthcare provider.**

5. Both the TST and IGRA **results are unreliable in infants who are 4-6 months of age or younger.** As with any patient, but especially important in young children, the interpretation of screening test results must be made in conjunction with epidemiology risk factors and a clinical assessment. **For infants younger than 6 months**, a negative TST or IGRA cannot be confirmed until the infant is 6 months old, or after the break in contact period, whichever is later.
    a. If the test is positive, then **refer** for medical evaluation.
    b. If negative, then **retest** at age 6 months or 8-10 weeks after the break in contact, whichever is later, to confirm a negative test.
        1) Any infant who is a contact to infectious tuberculosis should be placed on window prophylaxis until the TST or IGRA can be confirmed. See **Attachment 7: *Medications***.

6. A **TST** may be used if the patient is unable to receive an IGRA or refuses phlebotomy.
    a. **Do NOT administer TST** if any of the following apply*. Contact the licensed healthcare provider for instructions.
        1) Allergy to any component of TUBERSOL or APLISOL or an anaphylactic or other allergic reaction/hypersensitivity to a previous test of tuberculin purified protein derivative (PPD)
        2) Severe reaction to previous TST such as ulceration, necrosis, blistering, bullae, anaphylaxis
        3) A documented history of treatment for TB infection or disease
        4) Extensive burns or eczema
    b. **If TST is performed**, provide instructions to the patient regarding care of the injection site, then read and interpret the TST result within 48 to 72 hours.

**From:http://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm114924.pdf and http://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm114912.pdf*

Definition of TST Reactions:

- **Negative reaction**: An induration less than the specified criteria based on risk factors shows either a lack of tuberculin sensitivity or a low-grade sensitivity that most likely is not caused by *Mycobacterium tuberculosis* complex (*M.tb)*. A negative test does not rule out the presence of TB.

- **Positive Reaction**: An induration greater than or equal to the specified criteria based on risk factors indicates infection with *M.tb*.

TST Interpretation:

1) An induration of **5 mm or more** is considered to be positive for:
   - HIV-infected persons
   - Recent contacts to a known TB case
   - Individuals with fibrotic changes on chest radiograph consistent with old TB
   - Persons with organ transplants and other immunosuppressed persons (such as taking the equivalent of greater than 15 mg/day prednisone for longer than 1 month or taking tumor necrosis factor-α antagonists)

2) An induration of **10 mm or more** is considered to be positive for:
   - Individuals from high-prevalence countries
   - Injection drug users
   - Residents and employees of high-risk congregate settings: correctional facilities, nursing homes and other healthcare or long-term care facilities, residential facilities for AIDS patients, and homeless shelters
   - Mycobacteriology laboratory personnel
   - Persons with high-risk clinical conditions: silicosis, diabetes mellitus, chronic renal failure, some hematologic disorders (e.g., leukemias and lymphomas), other specific malignancies (e.g., carcinoma of the head or neck and lung), weight loss of > 10% of ideal body weight, gastrectomy, jejunoileal bypass
   - Children younger than 5 years of age.
   - Infants, children, adolescents exposed to adults in high-risk categories

3) An induration of **15 mm or more** is considered to be positive for:
   - Individuals with no known risk factors for tuberculosis.

ATTACHMENT 4: Laboratory Tests (Labs)

A. ***Patients suspected or confirmed to have TB disease*** age 18 or older, will have the following labs collected under the following circumstances:

At Baseline:

1. Measurements of complete blood count (CBC).

2. Liver function tests to include at least: AST, ALT, total bilirubin, alk phos, albumin, and creatinine.

Monthly:

1. Measurements of CBC if the baseline result is abnormal.

2. Measurements of AST, ALT, total bilirubin, and alk phos for patients whose baseline results are abnormal, and/or those with risk factors for hepatotoxicity or other complications, including but not limited to:
    a. Pregnant patients
    b. Female patients during the first three months postpartum
    c. Patients with or at risk for HBV, HCV, or other liver disorder
    d. Patients taking medications for other comorbidities or chronic medical conditions that may affect the liver or kidneys
    e. Patients who use alcohol or recreational drugs (orally or by injection)
    f. Patients with HIV infection/AIDS
    g. Patients on medications that affect or are excreted by the liver

As Needed:

1. Measurement of AST, ALT and total bilirubin if:
    a. AST, ALT level exceeds **more than three times** the upper limit of normal **in the presence of symptoms** or
    b. AST, ALT level exceeds more than **five times the upper limit** of normal **with or without symptoms** present, or
    c. Bilirubin exceeds **two times the upper limit** of normal.

    Hold medication and contact the licensed healthcare provider for instructions.

2. Measurements of a CMP and CBC if signs or symptoms are compatible with hepatotoxicity, including nausea or vomiting. Hold medication and contact the licensed healthcare provider.

3. Therapeutic drug monitoring for patients who are slow to respond to therapy and/or who have risk factors for poor drug absorption as determined by the licensed healthcare provider. Refer to *Therapeutic Drug Monitoring Process* at:

https://www.dshs.texas.gov/sites/default/files/LIDS-TB/forms/TherapeuticDrugMonitoringProcess.pdf.

Note: **Routine testing of serum uric acid is not recommended.** Acute gouty arthritis is a known adverse effect of pyrazinamide (PZA) and is rare except in patients with preexisting gout, which is generally a contraindication to the use of the drug. Non-gouty polyarthralgia may occur in up to 40% of patients receiving daily doses of PZA and rarely requires dosage adjustment or discontinuation of the drug. Asymptomatic hyperuricemia is an expected effect of the drug and is generally without adverse consequence. See http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm for additional information. If the patient develops signs and symptoms consistent with acute gouty arthritis, hold medication and contact the licensed healthcare provider for instructions.

B. ***Patients receiving treatment for TB infection (including patients on window prophylaxis) age 18 or older*** will have the following labs collected under the following circumstances:

At Baseline:

1. Measurements of AST, ALT, total bilirubin, alk phos, and albumin for all patients starting treatment for TB infection **AND** who have risk factors for potential hepatotoxicity or other complications, including but not limited to:
    a. Pregnant patients
    b. Female patients during the first 3 months postpartum
    c. Patients with or at risk for HBV, HCV, or other liver disorders
    d. Patients with other comorbidities or chronic medical conditions
    e. Patients who use alcohol or recreational drugs (orally or by injection)
    f. Patients with HIV infection/AIDS
    g. Patients on medications that affect or are excreted by the liver

2. Measurement of a complete blood count (CBC) if starting on a rifamycin.

Monthly:

1. Measurements of AST, ALT, total bilirubin, and/or alk phos if the baseline result is abnormal.

2. CBC if patient will be taking a regimen that includes a rifamycin, if the baseline CBC is abnormal.

3. Measurements of AST, ALT, total bilirubin, and alk phos for patients with risk

factors for hepatotoxicity or other complications, including but not limited to:

a. Pregnant patients
b. Female patients during the first three months postpartum
c. Patients with or at risk for HBV, HCV, or other liver disorder
d. Patients with other comorbidities or chronic medical conditions
e. Patients who use alcohol or recreational drugs (orally or by injection)
f. Patients with HIV infection/AIDS
g. Patients on medications that affect or are excreted by the liver

As Needed:

1. Measurement of AST, ALT and total bilirubin if:
    a. AST, ALT level exceeds **more than three times** the upper limit of normal **in the presence of symptoms** or
    b. AST, ALT level exceeds more than **five times the upper limit** of normal **with or without symptoms** present, or
    c. Bilirubin exceeds **two times the upper limit** of normal.

    Hold medication and contact the licensed healthcare provider for instructions.

2. Measurement of CMP and CBC if signs or symptoms are compatible with hepatotoxicity, including nausea or vomiting. Hold medication and contact the licensed healthcare provider.

NOTE: **For patients younger than 18 years**, considerations can be made for laboratory testing of children who meet the following criteria: chronic medical conditions, those on medications chronically, those with increased body mass index (BMI), pregnancy, disseminated disease or who endorse substance use. Contact the licensed healthcare provider. Note: alk phos varies in children depending on growth cycles, ensure that consideration is made for interpreting pediatric laboratory values.

ATTACHMENT 5: Chest X-Ray (CXR)

For patients younger than 18 years old, or patients with HIV infection, CXR should include posterior-anterior and lateral views.

For adult patients, CXR should include at least posterior-anterior view.
For pregnant patients evaluated for active TB disease, CXR should be done without delay and with appropriate shielding, even in the first trimester, if indicated.

A. <u>The following patients will have an initial CXR:</u>

1. **Patients suspected or confirmed to have TB disease:**
   a. All patients exhibiting signs and symptoms of active pulmonary TB disease.
   b. Patients with suspected or known extra-pulmonary TB to assess for the presence of pulmonary involvement.

2. **Patients with TB infection:**
   a. Patients exhibiting signs and symptoms of active pulmonary TB disease.
   b. Patients newly identified as infected with TB based upon a documented positive TST result or documented positive IGRA result.

3. **Patients undergoing evaluation as part of a contact investigation:**
   a. Patients exhibiting signs and symptoms of active pulmonary TB disease.
   b. Patients newly identified as infected with TB based upon a documented positive TST result or documented positive IGRA result.
   c. Patients who are contacts to a TB case and have documentation of a prior positive TB screening test but have not been treated for TB infection.
   d. Patients* who are contacts to a TB case and who are at high risk of progression to active TB disease ***regardless of their TB screening test result*** and ***regardless of prior treatment for TB infection/disease***:
      1) Children younger than 5 years old
      2) Patients who have HIV infection or at high risk for HIV infection
      3) Patients with an immunocompromising condition, such as being on dialysis
      4) Patients receiving immunosuppressive therapy
   e. Patients who have a previous CXR showing pulmonary fibrotic lesions (presumed from prior TB) and have not been treated for TB.

**These patients may be recommended for re-treatment. Contact the licensed healthcare provider.*

4. **Patients who have been referred to the health department for evaluation through the Electronic Disease Notification (EDN) system (excluding status adjusters) or who have self-referred for services,**

when indicated. EDN patients needing an *initial* CXR include:

a. Any patient with signs and symptoms of TB disease
b. Any patient with a positive IGRA or TST on **domestic** screening
c. All patients with known HIV infection
d. Any patient classified as a Class A or B* whose overseas medical examinations are unavailable and/or there has been a change in clinical status (i.e., new signs or symptoms of pulmonary or extrapulmonary TB disease)
e. Any EDN patient *as determined by the licensed health care provider*

**Some providers may recommend repeating radiology domestically for any patient with Class A or B TB classification if the CXR was performed overseas; contact the licensed healthcare provider.*

For full guidelines on screening immigrants referred from the Electronic Disease Notification (EDN), see: https://www.cdc.gov/immigrant-refugee-health/hcp/domestic-guidance/tuberculosis.html?CDC_AAref_Val=https://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/tuberculosis-guidelines.html.

5. **Asymptomatic pregnant females with a positive TST or IGRA.**
   a. CXR may be deferred until after the first trimester unless the patient has one or more of the following, in which case perform a CXR **with a lead shield over the abdomen** without delay:
      1) HIV or other immunosuppression
      2) History of recent contact with a person with infectious TB disease
      3) Documented TB infection test conversion in the past 2 years.
   b. In general, if a CXR was done in the 3 months prior to the medical evaluation, its findings were documented as normal, and the person is asymptomatic, then a repeat CXR is not necessary.
   c. For all other asymptomatic patients with a positive TB test, the CXR may be deferred to the second trimester; do not delay until the third trimester.

B. The following patients will have a follow-up CXR:

1. Patients suspected or confirmed to have TB disease:
   a. For all patients who started medication for TB, regardless of culture results, obtain a CXR at completion of 2 months of treatment.
   b. All patients should have a CXR near or at the end of treatment to serve as a new baseline for future evaluations, unless a previous CXR is negative.
   c. When therapy is interrupted. Contact the licensed healthcare provider when:
      1) There is concern for worsening or progression of illness, or
      2) treatment must be re-started.

If any of the following apply, **do not obtain a follow-up CXR**:

1) If a previous CXR (baseline or at 2 months) is negative, an end of treatment CXR is not necessary.
2) Follow-up CXRs are not necessary for patients with extrapulmonary TB disease, if initial sputum collection results are negative and initial CXR is normal.

2. **Patients with TB infection (including patients on window prophylaxis):**
   a. Patients who report or begin to exhibit symptoms suggestive of TB disease should have a follow-up CXR before continuing treatment for TB infection.
   b. Patients who have *not started treatment* for TB infection *within one month* of the initial CXR showing no abnormalities suggestive of TB disease AND are at high risk of progression to active TB disease must have a repeat CXR showing no abnormalities suggestive of TB disease prior to the initiation of therapy.

      The following patients are at **high risk of progression to** TB disease:

      1) Children younger than 5 years of age
      2) Patients who have HIV infection or at high risk for HIV infection
      3) Patients who have an immunocompromising condition or other clinical condition that is associated with progression to active TB (such as substance abuse, silicosis, underweight by more than 5%, diabetes, chronic renal failure, gastrectomy, jejunoileal bypass, solid organ transplantation, head and neck cancer)
      4) Patients receiving immunosuppressive therapy
      5) Patients within groups having high rates of TB transmission [homelessness, injection drug users] or within groups who work or reside with people who are at high risk for TB in facilities or institutions [hospitals, homeless shelters, correctional facilities, nursing homes, residential homes for those with HIV])
      6) Patients* without TB signs and symptoms who have a documented change in TB screening test results from a negative to positive and other patients who have been recently infected with TB such as:
         i. Close contacts close contacts of a person with infectious TB disease.
         ii. Patients who have immigrated from areas of the world with high rates of TB.
      7) Patients* without TB signs and symptoms with pulmonary fibrotic lesions seen on CXR (presumed to be from prior, untreated TB).

**for patients listed in 6 and 7 above, do not delay treatment if obtaining a repeat CXR would significantly delay care. If needed, start therapy while awaiting CXR coordination.*

c. Patients who have an *interruption* in TB infection treatment *longer than one month during the first 2 months of treatment* AND are at high risk of progression to active TB disease (see list above) must have a repeat CXR showing no abnormalities suggestive of TB disease prior to the re-initiation of therapy. Otherwise, reimaging is not necessary unless the patient has symptoms consistent with active TB disease.
d. All other patients who are not at high risk of progressing to active TB disease who have *not started treatment for TB infection* ***within 6 months*** of the initial CXR showing no abnormalities suggestive of TB disease must have a repeat CXR showing no abnormalities suggestive of TB disease prior to the initiation of therapy.
e. All other patients who are not at high risk of progressing to active TB disease who have an *interruption* in TB infection treatment ***and treatment needs to be re-started must have a repeat CXR*** showing no abnormalities suggestive of TB before therapy is re-started.

ATTACHMENT 6: Sputum Collection

When possible, all sputum specimens should be mailed to the laboratory on cold packs in order to preserve the specimen as long as possible. Refer to *Tuberculosis Specimen Shipping Guide* at: www.texastb.org

When collecting consecutive sputum specimen, they should be:

- ideally 24 hours apart, but at minimum 8 hours apart
- with at least one specimen collection observed
- with at least one specimen collection in early morning
- ideally with no more than 96 hours between the first and the third sputum specimen collection.

A. *Patients suspected or confirmed to have PULMONARY TB disease:*

1. For all patients, collect 3 consecutive sputum specimens. Sputum collection must occur within 7 days before (preferable) to 7 days after drug start date.
   a. Submit 3 sputum specimens for acid-fast bacilli (AFB) smear and culture.
      1) The DSHS laboratory will perform drug susceptibility testing (DST) reflexively on the initial *M.tb* culture positive specimen.
      2) The DSHS laboratory will repeat the DST if the patient is still *M.tb* culture-positive 3 months or more after the initial specimen collection date, or upon physician request.
   b. For all patients who have no laboratory confirmation of a rapid test that shows rifampin resistance (i.e., GeneXpert), regardless of positive *M. tb* cultures, request nucleic acid amplification testing (NAA)* **unless drug susceptibility test (DST) results are known**.
      1) Label the initial specimens "1 of 3," "2 of 3," and "3 of 3"
      2) The DSHS laboratory will perform NAA on only the most suitable specimen.
   c. For patients who have an *initial* **AFB sputum smear positive** result and the **NAA* is negative**, the DSHS laboratory will reflexively perform a second NAA on a second AFB smear positive specimen, if it is available.
      1) Repeat NAAs will only be performed if that second specimen is AFB smear positive.
      2) If a second AFB sputum smear positive specimen is not available, contact the licensed healthcare provider if a repeat NAA order is needed to develop a treatment plan.

2. For patients who have positive initial AFB smears at the time of diagnosis, collect 3 sputum specimens, with at least one specimen collection in early morning, for AFB smear every 2 weeks until 3 consecutive specimens are negative on AFB smear.

3. For all patients, collect up to 3 sputum specimens, with at least one specimen collection in early morning, for AFB smear and culture at least once a month until 2 consecutive specimens (at least one month apart) are negative on culture and there are no further positive cultures. *At this point, the patient has reached culture conversion.*

4. For patients who have completed < 80% of planned doses in the continuation phase of TB treatment and have an interruption of therapy, collect 3 sputum specimens, with at least one specimen collection in early morning, for AFB smear and culture. Refer to Attachment 7, F. ***Interruptions of Therapy for TB Disease***, for further guidance.

5. For patients with MDR-TB, after culture conversion, continue to collect at least one sputum specimen for AFB smear and culture, with at least one specimen collection in early morning, at least once a month, until treatment completion.

6. For all patients, if possible, collect one final sputum specimen in early morning for AFB culture at completion of therapy.

B. ***Patients confirmed to have EXTRAPULMONARY TB disease:***

1. For patients with suspected or known extrapulmonary TB, attempts should be made to collect 3 consecutive sputum specimens, even if the CXR is normal, in order to exclude concomitant pulmonary disease.
   a. Submit 3 sputum specimens for AFB smear and culture.
      1) The DSHS laboratory will perform DST reflexively on the initial *M.tb* culture-positive specimen.
      2) The DSHS laboratory will repeat the DST if the patient is still *M.tb* culture positive 3 months or more after the initial specimen collection date, or upon physician request.
   b. For all patients who have no laboratory confirmation of a rapid test that shows rifampin resistance (i.e., GeneXpert), regardless of positive *M. tb* cultures, request NAA* **unless drug susceptibility test (DST) results are known**.
      1) Label the initial specimens "1 of 3," "2 of 3," and "3 of 3"
      2) The DSHS laboratory will perform NAA on only the most suitable specimen.

2. For patients whose initial sputum results are positive, collect follow-up sputum as described in section A. *Patients suspected or confirmed to have PULMONARY TB disease.*

3. **For patients with suspected or known extrapulmonary involvement:** If Gastrointestinal (GI) or genitourinary (GU) TB is suspected, stool or urine samples can be collected in addition to sputum (as above) and sent for NAA test, AFB smear and culture. In addition, any specimen collected on an extrapulmonary site, including cerebral spinal fluid (CSF), aspirates from a lymph node or pleural fluid, peritoneal fluid, and an aspirate from purulent collection or biopsy site should be submitted for AFB smear, culture and NAA. Coordinate with the receiving laboratory and contact DSHS state laboratory for submission criteria prior to shipping. See: http://www.dshs.texas.gov/lab/myco_home.shtm.

**For interpretation and response to NAA test results, refer to Figure 1, below.*

C. *Patients with TB infection (including patients on window prophylaxis):*

1. For patients who develop signs and symptoms suggestive of TB disease, collect 3 consecutive sputum specimen.
   a. Submit 3 sputum specimens for AFB smear and culture.
      1) The DSHS laboratory will perform DST reflexively on the initial *M.tb* culture-positive specimen.
      2) The DSHS laboratory will repeat the DST if the patient is still *M.tb* culture positive 3 months or more after the initial specimen collection date, or upon physician request.
   b. For all patients who have no laboratory confirmation of a rapid test that shows rifampin resistance (i.e., GeneXpert), regardless of positive *M. tb* cultures, request NAA* **unless drug susceptibility test (DST) results are known**.
      1) Label the initial specimens "1 of 3," "2 of 3," and "3 of 3"
      2) The DSHS laboratory will perform NAA on only the most suitable specimen.

2. For patients with CXR findings suggestive of prior, healed TB disease, collect 3 consecutive sputum specimens.
   a. Submit 3 sputum specimens for AFB smear and culture.
      1) The DSHS laboratory will perform DST reflexively on the initial *M.tb* culture-positive specimen.
      2) The DSHS laboratory will repeat the DST if the patient is still *M.tb* culture positive 3 months or more after the initial specimen collection date, or upon physician request.
   b. For all patients who have no laboratory confirmation of a rapid test that shows rifampin resistance (i.e., GeneXpert), regardless of positive *M. tb* cultures, request NAA* **unless drug susceptibility test (DST) results are known**.

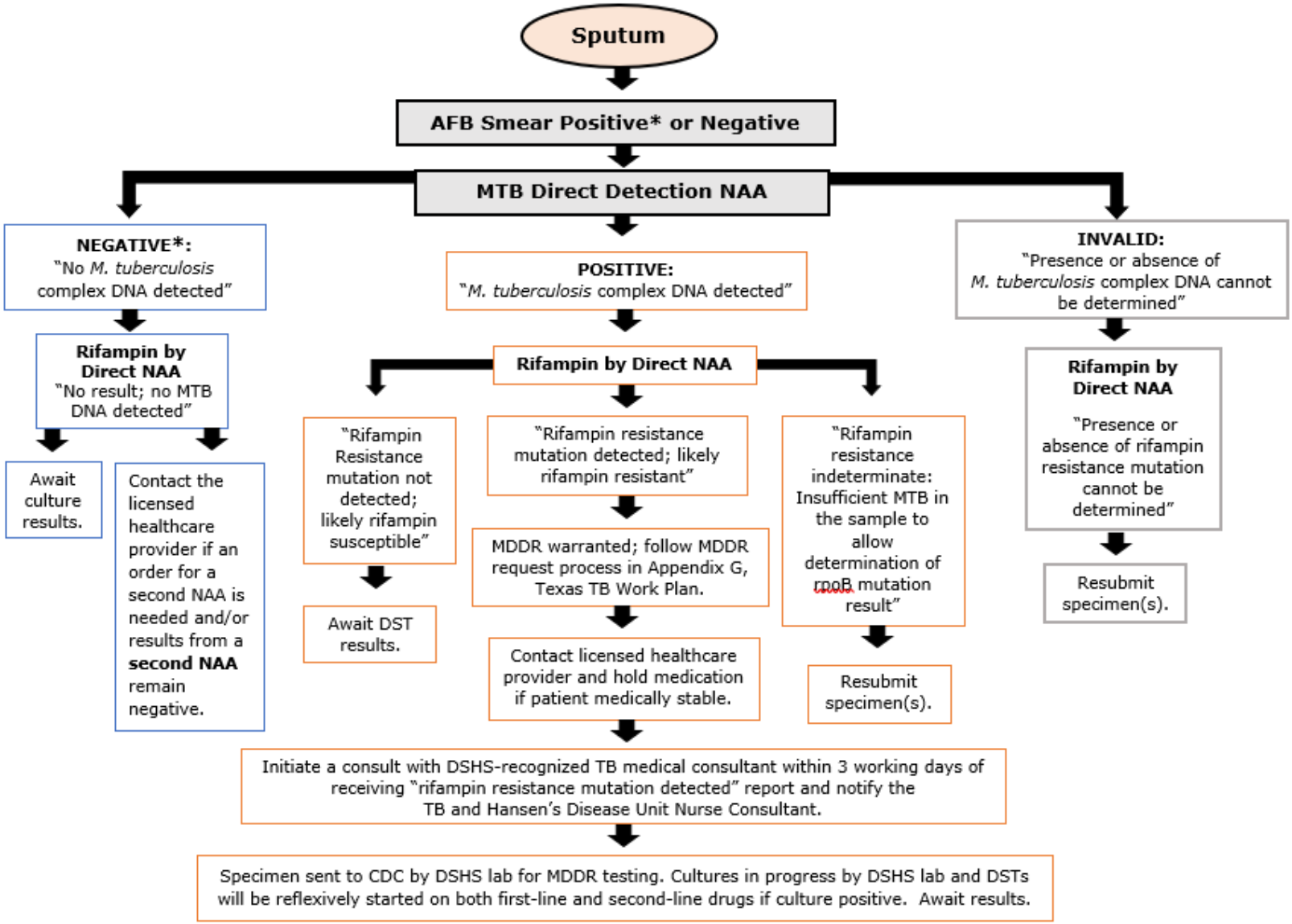
1) Label the initial specimens "1 of 3," "2 of 3," and "3 of 3"
2) The DSHS laboratory will perform NAA on only the most suitable specimen.

c. Results of all AFB smears and cultures must be negative before treatment for TB infection is started.

3. For patients with HIV infection referred through a civil surgeon (i.e., status adjusters) and/or all patients with HIV infection *and* respiratory symptoms, even if the CXR is normal, prior to the initiation of therapy, collect 3 consecutive sputum specimens.
   a. Submit 3 sputum specimens for AFB smear and culture. The DSHS laboratory will perform DST reflexively on the initial *M.tb* culture-positive specimen. The DSHS laboratory will repeat the DST if the patient is still *M.tb* culture positive 3 months or more after the initial specimen collection date, or upon physician request.
   b. For all patients who have no laboratory confirmation of a rapid test that shows rifampin resistance (i.e., GeneXpert), regardless of positive *M. tb* cultures, request NAA* **unless drug susceptibility test (DST) results are known**.
      1) Label the initial specimens "1 of 3," "2 of 3," and "3 of 3"
      2) The DSHS laboratory will perform NAA on only the most suitable specimen.
   c. **Results of all AFB smears and cultures must be negative and respiratory symptoms must be explained by another etiology before treatment for TB infection is started**.

**For interpretation and response to NAA test results, refer to Figure 1, below.*

Figure 1: *Interpretation and Response to Nucleic Acid Amplification (NAA) Test Results*



Acronyms: MTB - Mycobacterium tuberculosis; DST - Drug Susceptibility Test; MDDR – Molecular Detection of Drug Resistance

*****If the initial specimen is AFB smear positive *and* NAA negative, DSHS laboratory will reflexively perform a second NAA on an additional AFB smear positive specimen if available.

ATTACHMENT 7: *Medications*

A. Drug regimens for patients suspected or confirmed to have TB disease:

Administer the following medications after verifying that a current order is written by the licensed healthcare provider; that order should be implemented within **3** business days, or a new order must be received. Tables 1-4 are for reference only and do not replace medication orders from the licensed healthcare provider.

TABLE 1. Drug Regimens for Culture-Positive Pulmonary TB caused by Drug-Susceptible Organisms

	Intensive Phase		Continuation Phase				
Regimen	**Drugs**	**Interval, Dose**	Regimen	**Drugs**	**Interval and Dose, Duration**	**Range of Total Doses** (duration)	**Comments**
1	INH, RIF‡, PZA*, EMB**	7 days/wk for **56** doses in 8 wks, or 5 days/wk for **40** doses in 8 weeks	**1a**	INH, RIF	**If 6 months' total therapy:** 7 days/wk for **126** doses in 18 wks or 5 days/wk for **90** doses in 18 wks	**182-130** (26 weeks)	**Preferred** regimen for patients with newly diagnosed tuberculosis.
			1b		**If 9 months' total therapy:** 7 days/wk for **217** doses in 31 wks or 5 days/wk for **155** doses in 31 wks	**273-195** (39 weeks)	
Medical Consultation is Required for Regimens 2 and 3, as Daily Dosing Is Preferred							
2	INH, RIF‡, PZA*, EMB**	7 days/wk for **56** doses in 8 wks, or 5 days/wk for **40** doses in 8 weeks	**2a**	INH, RIF	**If 6 months' total therapy:** 3 times/wk† for **54** doses in 18 wks	**110-94** (26 weeks)	**May be considered in rare cases** when daily DOT in the continuation phase is not possible.
			2b		**If 9 months' total therapy:** 3 times/wk† for **93** doses in 31 wks	**149-133** (39 weeks)	
3†	INH, RIF‡ PZA* EMB**	3 times weekly for **24** doses in 8 weeks	**3a**	INH, RIF	***If 6 months' total therapy:*** 3 times/wk† for **54** doses in 18 wks	**78** (26 weeks)	Use with caution in patients with HIV and/or cavitary or extensive disease.
			3b		***If 9 months' total therapy:*** 3 times/wk† for **93** doses in 31 wks	**117** (39 weeks)	

Table 1. *Continued*

Definition of abbreviations: **INH** = Isoniazid; **RIF** = Rifampin; **PZA** = Pyrazinamide; **EMB** = Ethambutol

*__PZA:__ may be stopped after the initial phase is complete (40 or 56 doses) *if* drug susceptibility testing is known. **PZA and advanced age:** The 2016 TB treatment guidelines recommend caution when treating adults of advanced age, stating: "The risk of drug-induced hepatitis and other serious adverse effects increases with advancing age because of less efficient drug elimination due to reduced renal and hepatic clearance. Because PZA is the most common culprit, the benefits of including PZA in the initial regimen for elderly patients with modest disease and low risk of drug resistance may be outweighed by the risk of serious adverse events…Careful clinical monitoring to detect intolerance and adverse reactions is warranted." Refer to page 36 for more details: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf

**__EMB:__ may be stopped if the isolate is susceptible to RIF and INH.

‡__RIF__: if rifampin cannot be used due to certain drug-drug interactions, **rifabutin (RBT) may be substituted for rifampin**. Rifabutin dosage is 5mg/kg with a maximum dose of 300mg PO daily, given as daily dosing (not to be used bi-weekly or thrice weekly). Patients weighing less than 30kg should be carefully dosed and monitored on rifabutin, which must be compounded. Seek medical consultation with a DSHS-Recognized TB Medical Consultant if dosing assistance is needed. For more information on rifabutin use, dosing, and drug/drug interactions, including rifabutin use for patients with HIV, refer to Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf.

†__Intermittent therapy of thrice-weekly dosing *may be considered* in individuals with low risk of relapse__ (i.e., drug-susceptible TB organisms, that at the start of treatment is non-cavitary and/or smear negative, and those who are HIV negative.) ***Consultation is required.***

Daily dosing is the preferred standard of care for all patients. Interventions to support daily dosing, including video DOT (VDOT), should be arranged, when possible, as intermittent dosing is less efficacious and leads to higher rates of relapse. Table 1 reflects regimens listed in order of preference. ***Consultation is required for dosing less than daily.***

Table originally adapted from Treatment of Tuberculosis. MMWR. 2003; 52(RR11) and includes updated guidelines from Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clinical Infectious Diseases (2016) 63 (7): e147-e195. https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf

TABLE 2. Doses of First-Line Anti-Tuberculosis Drugs for ADULTS

Daily Dosing				
Weight (kg) *Based on estimated lean body weight* ¥	**Isoniazid*** **(INH)** Dose, mg (mg/kg)	**Rifampin**** **(RIF)** Dose, mg (mg/kg)	**Pyrazinamide (PZA)** Dose, mg (mg/kg)	**Ethambutol (EMB)** Dose, mg (mg/kg)
40-55 kg	300† mg (5mg/kg)	600 mg (10-20mg/kg‡)	1,000 mg (18.2–25.0)	800 mg (14.5–20.0)
56-75 kg			1,500 mg (20.0–26.8)	1,200 mg (16.0–21.4)
76-90 kg			2,000† mg (22.2–26.3)	1,600† mg (17.8–21.1)
Thrice (3x) Weekly Dosing – *Consultation Required*				
Weight (kg) *Based on estimated lean body weight* ¥	**Isoniazid*** **(INH)** Dose, mg (mg/kg)	**Rifampin**** **(RIF)** Dose, mg (mg/kg)	**Pyrazinamide (PZA)** Dose, mg (mg/kg)	**Ethambutol (EMB)** Dose, mg (mg/kg)
40-55 kg	900† mg (15mg/kg)	600 mg (10-20mg/kg)	1,500 mg (27.3–37.5)	1,200 mg (21.8–30.0)
56-75 kg			2,500 mg (33.3–44.6)	2,000 mg (26.7–35.7)
76-90 kg			3,000† mg (33.3–39.5)	2,400† mg (26.7–31.6)
Forms available	**Scored tablets:** 100 mg, 300 mg and Syrup (50mg/5ml)	**Capsule:** 150 mg, 300 mg *Contact DSHS for compounding*	**Scored tablets:** 500 mg	**Tablets**: 100 mg, 400 mg

*__Isoniazid:__ Supplementation with pyridoxine (vitamin B6) 25-50 mg daily is recommended in the following: pregnant women, infants receiving INH and breastfeeding, patients with diets likely deficient in pyridoxine, patients with paresthesia, patients age ≥65 years or patients who have a risk factor for paresthesia (e.g., HIV/AIDS, alcohol use, diabetes).

**__Rifampin:__ Drug interactions with potentially serious consequences may occur when using Rifampin. Of particular concern are reductions, often to ineffective levels, in serum concentrations of common drugs, such as oral contraceptives, methadone, and warfarin. There are important bidirectional interactions between rifamycins and antiretroviral agents. Because information regarding rifamycin drug interactions is evolving rapidly, consult a trusted drug information resource to obtain the most up-to-date information.

‡__Rifampin Dosing:__ Many experts recommend using a **daily rifampin dose of 20-30mg/kg/day** for adults and children with serious forms of TB (i.e., meningitis, disseminated TB). See American Academy of Pediatrics Red Book, 2021, 32nd Ed. Consult recommended. If using **rifabutin** instead of rifampin, **rifabutin dosage is 5mg/kg with a maximum dose of 300mg PO daily**, given as daily dosing (not to be used bi-weekly or thrice weekly).

†__Maximum dose regardless of weight__, unless otherwise recommended by a DSHS Recognized TB Medical Consultant.

¥__Dosing based on actual weight is acceptable in patients who are not obese.__ For obese patients (>20% above ideal body weight [IBW]), dosing based on IBW may be preferred for initial doses. Some clinicians prefer a modified IBW (IBW + [0.40 × (actual weight – IBW)]) as is done for initial aminoglycoside doses. Consider therapeutic drug monitoring for obese patients.

Table adapted from Treatment of Drug-Susceptible Tuberculosis 2016 ATS/CDC/PIDS America Clinical Practice Guidelines. https://www.cdc.gov/tb/publications/guidelines/pdf/Clin-Infect-Dis.-2016-Nahid-cid_ciw376.pdf. PZA, EMB dose ranges from Heartland National TB Center and The Spectrum of Tuberculosis from Infection to Disease, TB at a Glance, 3rd Edition. https://www.heartlandntbc.org/products/.

TABLE 3. PEDIATRIC (age 17 and younger) Dosing Range for Daily, Maximum Doses, and Forms Available for First-Line Anti-Tuberculosis Drugs

Daily Dose Range*					
Child's Weight (kg)	**Isoniazid (INH)** 10-15 mg/kg Dose, mg Max dose: 300mg	**Pyrazinamide (PZA)** 30-40 mg/kg Dose, mg Max dose: 2000mg	**Ethambutol (EMB)** 15-25 mg/kg Dose, mg Max dose: 1000mg	**Rifampin (RIF) ≥2 years** 15-20 mg/kg Dose‡, mg Max dose: 600mg	**Rifampin (RIF) <2 years** 20-30 mg/kg Dose‡, mg Max dose: 600mg
3-5	50 mg	125 mg	50-100 mg	50-75 mg	75-100 mg
6-9	100 mg	250 mg	150 mg	100-150 mg	150-200 mg
10-15	150 mg	375-500 mg	250 mg	150-300 mg	200-300 mg
16-20	200 mg	500-750 mg	300 mg	300 mg	450 mg
21-25	300 mg	750 mg	400 mg	300-450 mg	450-600 mg
26-30	300 mg	1000	600-700 mg	450-600 mg	600 mg
31-45	300 mg	1250-1500	800 mg	600 mg	600 mg
46-50	300 mg	1500-2000 mg	1000 mg	600 mg	600 mg
50+	300 mg	2000 mg	1000 mg	600 mg	600 mg
Forms available	**Scored tablets:** 100 mg and 300 mg **Syrup†:** 50 mg/5ml	**Scored tablets:** 500 mg	**Tablets:** 100 mg and 400 mg	**Capsules:** 150 mg and 300 mg **Suspension:** *Contact DSHS Pharmacy*	

NOTE: There are many factors that can affect medication stability when tablets are broken or crushed/capsules are opened and then mixed with food or liquids. Consult a trusted drug reference before using food disguises.

*Table 3 reflects doses for daily dosing but "*the optimal doses for thrice-weekly therapy in children have not been established. Some experts use in adolescents the same doses as recommended for adults, and for younger children the same doses as recommended for twice-weekly therapy*" (https://www.cdc.gov/tb/publications/guidelines/pdf/Clin-Infect-Dis.-2016-Nahid-cid_ciw376.pdf). Seek medical consultation, as thrice weekly dosing requires a consult.

†Many experts advise against using INH syrup because it is frequently associated with diarrhea.

‡Specialty compounding is needed for doses not commercially available. Contact DSHS pharmacy when compounding is indicated. If using **rifabutin** instead of rifampin, **rifabutin dosage is 5mg/kg with a maximum dose of 300mg PO daily**, given as daily dosing (not to be used bi-weekly or thrice weekly). Patients weighing less than 30kg should be carefully dosed and monitored on rifabutin, which must be compounded. Seek medical consultation if dosing assistance is needed.

Table adapted from Kim Connelly Smith, MD, MPH, The University of Texas-Houston McGovern Medical School

B. Alternate short-course regimen for children with non-severe, drug susceptible TB:

1. An alternate short-course TB regimen called **SHINE** may be used in children with non-severe drug-susceptible TB. Consider this regimen for children with minimal disease. Many children identified through screening activities such as a contact investigation or others recently infected may be good candidates for this regimen as well as those listed below.

   a. **SHINE may be used in the following groups of children:**
   - Age 3 months to 16 years, weighing ≥3 kg
   - Diagnosed with known or suspected drug susceptible pulmonary TB (child should have no known or suspected drug resistance)
   - May be symptomatic, but not severe
   - Have non-severe TB defined as:
     - pulmonary TB that is confined to one lobe
     - isolated intrathoracic adenopathy
     - peripheral lymph node TB
     - no cavities
     - no signs of miliary tuberculosis,
     - no complex pleural effusion
     - no clinically significant airway obstruction
   - Acid-fast bacilli (AFB) smear negative **if** respiratory specimen were collected (i.e., sputum, via natural production or gastric aspirates)
     - May be NAA positive or negative
   - If lymphatic disease is known or suspected, a lymph aspirate may or may not be AFB smear positive.
   - On antiretroviral therapy (ART), if HIV positive
   - Successfully completed TB therapy >2 years prior to the new diagnosis, if previously treated for TB

   b. **SHINE may NOT be used in the following groups of children:**
   - Premature (<37 weeks) and under age 3 months
   - If sputum was collected, AFB smear-positive respiratory sample
   - Have miliary TB, spinal TB, TB meningitis, or have osteoarticular, abdominal or congenital TB
   - Have known or suspected drug-resistant TB (DR-TB), including contact to DR-TB
   - Are pregnant, severely ill, or who have contraindications to any of the anti-TB drugs

2. Dosing and treatment completion: 17 weeks total.
    a. **Initial Phase:** two months (8 weeks) of daily therapy with 3 – 4 drugs (rifampin, isoniazid, pyrazinamide, and with or without ethambutol [based on the drug sensitivities of the presumed source case]).
    b. **Continuation Phase**: two additional months (9 weeks) of daily rifampin and isoniazid.
    c. **Dosing and DOT**: Refer to table 3 for pediatric dosing.
        - **Option 1**: DOT 7 days per week totaling **119 doses** (17 weeks).
        - **Option 2**: DOT 5 days per week totaling **85 doses** and **34 doses** of self-administered medications, totaling 119 doses (17 weeks).

Table 4: SHINE Regimen for Children with Non-Severe TB

Intensive Phase*		**Continuation Phase****			
Drugs	**Interval, Dose**	**Drugs**	**Interval, Dose**	**Total Weeks**	**Comments**
INH, RIF, PZA, EMB†	7 days/week for **56** DOT doses in 8 weeks Or 5 days/week for **40** DOT doses (and **16** self-administered doses) in 8 weeks	INH, RIF	7 days/week for **63** DOT doses in 9 weeks Or 5 days/week for **45** DOT doses (and **18** self-administered doses) in 9 weeks	**119** (17 weeks)	This regimen should be administered by DOT either in person or through approved electronic enabled applications. If DOT is only possible M-F, provide self-administered medications on weekends.

*When any interruption of 14 or more *cumulative* days occurs in the **initial phase** of treatment for TB disease, the treatment regimen will need to be restarted. Contact the licensed healthcare provider for instructions.

The **continuation phase must be administered within 84 days from intensive phase completion so that the regimen is completed within 5 months. If there is an interruption and patient will not meet that target, contact the licensed healthcare provider.

†This regimen is for children with non-severe TB, often identified in a TB contact investigation. **EMB** should be included in the initial phase *if* the presumed source case DSTs are unknown. If DSTs are known and the source case is susceptible to RIF and INH, EMB is not required. Seek consultation if necessary.

The SHINE TB regimen is based on clinic trial data[1] and detailed in American Academy of Pediatrics (AAP) *Red Book: 2024- 2027 Report of the Committee on Infectious Diseases, 33rd ED.* https://publications.aap.org/redbook/book/755/Red-Book-2024-2027-Report-of-the-Committee-on?autologincheck=redirected

[1]Turkova A, Wills GH, Wobudeya E, *et al*. Shorter treatment for non-severe tuberculosis in African and Indian children. *N Engl J Med* 2022;386:911–922. https://ep.bmj.com/content/early/2022/09/06/archdischild-2022-324395

C. Provide established regimens for patients with latent TB infection (including patients on window prophylaxis):

Administer the following medications after verifying a current order is written by the licensed healthcare provider.

Table 5. Recommended Drug Regimens for Treatment of INH-and RIF-Susceptible Latent TB Infection

Drugs	Duration	Dose	Frequency	Total Doses For Completion of Therapy
Isoniazid* and Rifapentine† (3HP) **Not** recommended for: -Children <2 years old - Patients with HIV taking antiretroviral therapy other than efavirenz- or raltegravir-based regimens -Patients who or expecting to become pregnant -Patients with TB infection or are contacts to a TB case that is resistant (or suspected to be) to INH or a rifamycin	3 months	**Adults and children ≥ 12 years:** **INH:** 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg max. **RPT:** 10.0–14.0 kg: 300 mg 14.1–25.0 kg: 450 mg 25.1–32.0 kg: 600 mg 32.1–49.9 kg: 750 mg ≥50.0 kg: 900 mg maximum **Children 2-11 years:** **INH:** 25 mg/kg rounded up to the nearest 50-100 mg; 900 mg max. **RPT:** 10.0–14.0 kg: 300 mg 14.1–25.0 kg: 450 mg 25.1–32.0 kg: 600 mg 32.1–49.9 kg: 750 mg ≥50.0 kg: 900 mg maximum **Children under age 2 years:** Contraindicated	**Once weekly,** ***DOT strongly preferred‡***	**12** doses (minimum of 11 doses acceptable) administered in no fewer than 12 weeks (but no more than 16 weeks) Doses must be separated by ≥72 hours to be counted
Rifampin† (4R) -preferred option during pregnancy	4 months	**Adults:** 10-20 mg/kg Maximum dose: 600 mg **Children ≥ 2ys-17ys**: 15-20 mg/kg Maximum dose: 600 mg **Infants** and **Toddlers <2ys**: 20-30mg/kg Maximum dose: 600mg	**Daily**	**120** (7 days/ week) OR **90** (for 5 days/week by DOT) within 6 months

Table 5. *continued*

Isoniazid[*] and Rifampin[†] (3HR)	3 months	**Adult:** **INH**: 5 mg/kg; Maximum dose: 300 mg **RIF**: 10 mg/kg Maximum dose: 600 mg **Children:** **INH:** 10-20 mg/kg[**]; Maximum dose: 300 mg **RIF:** 15-20 mg/kg; Maximum dose: 600 mg	**Daily**	**90** (7days/week) within 4 months
Isoniazid[*] (6H/9H)	6 months	**Adult:** 5 mg/kg Maximum dose: 300 mg **Children:** 10-20 mg/kg[**] Maximum dose: 300 mg	**Daily**	**180** (7 days/ week) OR **129** (for 5 days/week by DOT) within 9 months
		Adult: 15 mg/kg Maximum dose: 900 mg **Children:** 20-40 mg/kg[**] Maximum dose: 900 mg	**Twice weekly[‡]**	**52** by DOT ONLY within 9 months
	9 months	**Adult:** 5 mg/kg Maximum dose: 300 mg **Children:** 10-20 mg/kg[**] Maximum dose: 300 mg	**Daily**	**270** (7 days/ week) OR **195** (for 5 days/week by DOT) within 12 months
		Adult: 15 mg/kg Maximum dose: 900 mg **Children:** 20-40 mg/kg[**] Maximum dose: 900 mg	**Twice weekly[‡]**	**76** within 12 months by DOT only

Table 5. *continued*

Definition of abbreviations: **INH** = Isoniazid; **RIF** = Rifampin; **RPT** = Rifapentine

NOTES:

- **Short course regimens are preferred to the 6 or 9-month INH regimens.**
- **LTBI therapy during pregnancy:** first-line TB drugs are considered safe in pregnancy and all LTBI regimens (with the exception of 3HP) can be used to treat LTBI in this population. All first-line TB drugs are found in breast milk at low levels. Patients can safely breastfeed while on any approved regimens for LTBI. While rifampin is the preferred LTBI therapy, rifabutin can also be used safely in pregnancy. Refer to: *Testing and Treatment of Latent Tuberculosis Infection in the United States, 3rd Edition*, for details. http://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/ and https://www.cdc.gov/tb/media/pdfs/Latent-TB-Infection-A-Guide-for-Primary-Health-Care-Providers.pdf.

*__INH:__ Supplementation with pyridoxine (vitamin B6) is recommended in the following: pregnant women, infants receiving INH and breastfeeding, patients with diets likely deficient in pyridoxine, patients with paresthesia, or patients who have a risk factor for paresthesia (e.g., HIV/AIDS, alcohol use, diabetes). NOTE: due to increased risk of hepatotoxicity during pregnancy and in the immediate post-partum period (first three months after delivery), INH monotherapy should be used with caution in pregnancy.

†__RIF, RPT:__ Both have drug interactions with potentially serious consequences. Of particular concern are reductions, often to ineffective levels, in serum concentrations of common drugs, such as oral contraceptives, methadone, and warfarin. There are important bidirectional interactions between rifamycins and antiretroviral agents. Because information regarding rifamycin drug interactions is evolving rapidly, consult a trusted drug information resource to obtain the most up-to-date information. **NOTE: Rifabutin (RBT) may be substituted for rifampin if rifampin cannot be used due to certain drug-drug interactions.** Rifabutin dosage is 5mg/kg with a maximum dose of 300mg PO daily, given as daily dosing (not to be used bi-weekly or thrice weekly). Patients weighing less than 30kg should be carefully dosed using a compounded form of rifabutin and require close monitoring. Seek medical consultation with a DSHS-Recognized TB Medical Consultant if dosing assistance is needed. For more information on rifabutin use, dosing, and drug/drug interactions, including rifabutin use for patients with HIV, refer to Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf.

The American Academy of Pediatrics recommends an **isoniazid dosage of 10-15mg/kg for the daily regimen and 20-30mg/kg for the twice-weekly regimen in children. For more details refer to *Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020*: https://www.cdc.gov/mmwr/volumes/69/rr/rr6901a1.htm?s_cid=rr6901a1_w&deliveryName=USCDCNPIN_151-DM19855 and American Academy of Pediatrics Red Book, 2021, 32nd Ed.

‡Intermittent regimens of INH mono therapy must be provided by directly observed therapy (DOT). It is recommended that 3HP also be administered via DOT unless specified by the licensed healthcare provider. Self-administration *may be considered* in select patients when DOT is not possible, and when mechanisms are in place to help patients adhere to treatment, as determined by the licensed healthcare provider. Refer to https://www.cdc.gov/mmwr/volumes/67/wr/mm6725a5.htm?s_cid=mm6725a5_w and https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w

Table adapted from Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020. MMWR 2020; RR-69. https://www.cdc.gov/mmwr/volumes/69/rr/rr6901a1.ht

D. *Indications for window prophylaxis for contacts to someone with confirmed or suspected TB disease:*

1. Children younger than 5 years old
    a. Note: Children <6 months old should continue window prophylaxis until they undergo a repeat a TB screening test at 6 months of age.
2. Patients with HIV infection*
3. Patients receiving immunosuppressive therapy for organ transplantation*
4. Patients taking TNF-α inhibitors*

Treatment for window prophylaxis should be started no later than 14 days after the contact is identified as a candidate for treatment. If treatment cannot begin within 14 days, contact the licensed healthcare provided.

**Indications for window prophylaxis WITH recommendations to complete a full course of treatment for TB infection (beyond the window period) even if a TB screening test administered ≥ 8 weeks after the end of exposure is negative.*

E. *Interruptions of Therapy for TB Disease:*

1. Address treatment interruptions early on. Contact the licensed healthcare provider when indicated. Follow these guiding principles when reviewing medication adherence and addressing treatment interruptions:
    a. Every doses counts and is necessary for the most effective therapy.
    b. Non-adherence is a significant risk factor for patients having unfavorable outcomes. Refer to: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6685538/.
    c. In general, the longer the interruption and the earlier the interruption occurs, the more serious the impact of the interruption.
    d. Patients can be at an increased risk of relapse when doses are missed in the initial and continuation phase.
    e. DOT doses should be counted daily and monitored weekly, ensuring the patient completes the recommended number of doses each week.
    f. While the number of planned doses must be considered, so too the duration of therapy must also be considered. For example, the initial phase of treatment cannot stop prior to 8 weeks even if the minimum number of doses is completed before that duration.
    g. See https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf for more information.

2. When any **interruption occurs in the initial phase**, the following applies:
    a. If any interruption of less than 14 *cumulative* days occurs *the treatment can continue.*

b. If total initial phase treatment is not completed in 10 weeks, the treatment needs to be restarted. Contact licensed healthcare provider for instructions.
c. When any interruption of 14 or more *cumulative* days occurs in the initial phase of treatment for TB disease, the regimen will need to be restarted. Contact the licensed healthcare provider for instructions.
    1) If treatment is discontinued for drug intolerances, the patient must be on an empiric regimen considered adequate (RIP [RIF, INH, PZA], RIE [RIF, INH, EMB], or RPE [RIF, PZA, EMB]) for doses to count towards completion of therapy.
    2) If susceptibilities are known and there is no resistance to INH, RIF, or a fluroquinolone (FQN), either levofloxacin or moxifloxacin, then once the patient is on *both* INH *and* RIF, or RIF and a FQN, doses can count towards completion of therapy.

3. When any **interruption occurs in the continuation phase**, this applies:
    a. If a patient misses a cumulative total of 3 months of doses during the continuation phase and less than 80% of planned doses in the continuation phase are completed, treatment will need to be restarted.
        1) Collect 3 sputum specimens for AFB smear and culture, perform a CXR, and contact the licensed healthcare provider for further instructions.
    b. If a patient misses a cumulative total of 3 months of doses during the continuation phase and 80% or more of planned doses in the continuation phase are completed, additional treatment may not be necessary. However, patients who initially had sputum smears positive for AFB should receive additional therapy. Contact the licensed healthcare provider.

F. *Interruptions of Therapy for TB Infection:*

1. When an interruption occurs during treatment for TB infection, a CXR should be obtained in accordance with ATTACHMENT 5: *Chest X-Ray.*
    a. If a CXR is indicated, an examination and symptom screen to rule out active TB disease are also required before restarting therapy.

2. If the patient has symptoms consistent with active TB disease, a symptom screen, physical examination, CXR, and collection of 3 sputum specimens (if sputum can be produced) are required. Active TB disease must be excluded *before* treatment for TB infection is restarted.

3. If the minimum number of doses cannot be completed within the maximum time frame allowed, as described in section G: *Completion of Therapy for TB Infection* of this attachment, treatment will need to be restarted from the beginning. Contact the licensed healthcare provider for instructions.

G. *Completion of Therapy for Drug Susceptible TB Disease:* Below are the ***minimum*** number of doses and duration required, based on regimens listed in *Table 1* and the corresponding time frames for acceptable completion of therapy. The goal is to complete all doses within 12 months.

1. Completion of therapy for drug-susceptible TB disease by duration:
    a. Six months* (26 weeks) is generally the minimum duration of treatment.
    b. Nine months* (39 weeks) is recommended for patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy (see additional indications in #4, below), and for those patients intolerant of PZA or with M. bovis disease.

**These durations accurately indicate the amount of time the drugs are given only if there are no interruptions in drug administration.*

2. Total DOT doses required for treatment completion, per phase:
    a. **Initial phase to total 8 weeks:** Initial phase must have documentation of completion before counting doses for the continuation phase.

Regimen*	Total DOT Doses For INITIAL PHASE Completion
1	7 days per week for **56** doses administered by DOT in 8 weeks, OR 5 days per week for **40** doses administered by DOT in 8 weeks
2	7 days per week for **56** doses administered by DOT in 8 weeks, OR 5 days per week for **40** doses administered by DOT in 8 weeks
3	3 times weekly for **24** doses administered by DOT in 8 weeks

    b. **Continuation phase to total 18 or 31 weeks (INH/RIF):** Doses for continuation phase should **not** be counted until initial phase treatment has been documented to be appropriately completed.

Regimen*	Total DOT Doses For CONTINUATION PHASE Completion
1a	7 days per week for **126** doses administered by DOT in 18 weeks OR 5 days per week for **90** doses administered by DOT in 18 weeks
1b	7 days per week for **217** doses administered by DOT in 31 weeks, OR 5 days per week for **155** doses administered by DOT in 31 weeks
2a	3 times weekly for **54** doses administered by DOT in 18 weeks
2b	3 times weekly for **93** doses administered by DOT in 31 weeks
3a	3 times weekly for **54** doses administered by DOT in 18 weeks
3b	3 times weekly for **93** doses administered by DOT in 31 weeks

**Refer to Table 1: Drug Regimens for Culture-Positive Pulmonary TB caused by Drug-Susceptible Organisms*

3. **When regimens vary from above** (i.e., are extended or change frequently) doses from each phase should be converted to "daily dose equivalents."
    a. Use the minimum numbers for daily dosing of each phase when making a determination of adequate number of doses to complete therapy.
    b. *For example, for 5 days per week dosing, 40 doses should be given for the initiation phase and 90 doses should be given for the continuation phase.*
        - If 3 times (thrice) weekly doses were administered, multiply total number of thrice weekly doses by 1.67 (because 5 days per week ÷ 3 doses per week = 1.67) to convert thrice weekly doses to daily dose equivalents.
        - Add all daily dose equivalents together to calculate the total daily doses given.
        - Numbers that are not whole numbers should be rounded down.

    Consult the licensed healthcare provider, the local and/or regional TB program manager, or the TB and Hansen's Disease Unit TB Nurse Consultant(s) for assistance, if needed.

4. **Exceptions to the length of therapy** described above:
    a. In patients with PZA intolerance in the initial phase (40 doses given 5 days/week by DOT or 56 doses given 7 days/week by DOT), or those with *M. bovis*, then the regimen should be provided for a minimum duration of 9 months.
        1) EMB may be discontinued only when the isolate is known to be susceptible to isoniazid and rifampin.
        2) INH and RIF must be provided for a total minimum duration of treatment of 9 months (39 weeks).
        3) NOTE: *M. bovis* is naturally resistant to PZA and treatment duration must extend to a minimum of 9 months (39 weeks).
    b. Patients with cavitation or extensive pulmonary TB disease on initial CXR and a positive culture at the time of completion of 2 months (8 weeks) of treatment are *at substantially increased risk of relapse*.
        1) The continuation phase for these patients is recommended to be prolonged to 7 months (31 weeks), to complete a total treatment period of 9 months (39 weeks).
        2) Some experts also prolong the continuation phase to 7 months even when the culture converts by 2 months if the patient has extensive disease and a slow clinical response and/or underlying chronic disease that increases risk of poor outcome or relapse (i.e., dialysis, TNF alpha therapy, malignancy).

c. The following extrapulmonary TB sites generally require a longer duration of treatment:
    1) Bone and joint: 9 months (39 weeks) of treatment recommended
    2) Meningitis: 9 - 12 months (39 - 52 weeks) of treatment recommended
    3) Disseminated/miliary TB: 9 - 12 months (39 - 52 weeks) of treatment recommended
    4) Any site that is slow to respond should be considered for prolongation of treatment

d. Culture-negative pulmonary TB:
Defined as symptomatic or radiographic improvement after 2 months of RIPE treatment in a patient for whom:
    - the clinical suspicion for active TB disease is high,
    - AFB cultures were collected and are negative, AND
    - an alternative diagnosis/etiology has not been found
        1) For adult patients, because of a potential for INH-resistance, treatment should be continued with INH, RIF, *AND ethambutol* for an additional 2 months to complete a total of 4 months (18 weeks) of treatment.
        2) For pediatric patients with no identifiable source case, treatment should be continued with INH, RIF, *AND ethambutol* for an additional 4 months (18 weeks) to complete a total of 6 months (26 weeks) of treatment.
        3) Ethambutol can be discontinued if the patient with culture-negative pulmonary TB is a contact to a case and the susceptibilities of that case are known and no resistance is detected.

e. Culture-negative extrapulmonary TB: treatment recommendations are determined by the licensed healthcare provider, preferably in consultation with a DSHS-recognized TB Medical Consultant.

f. Patients newly diagnosed with HIV who are not started on anti-retroviral therapy (ART) during treatment for TB: treatment should consist of at least 8+ months of therapy or longer.

g. If RIF cannot be included in the treatment regimen, a drug-resistant TB regimen must be provided. **Medical consultation required.**

H. ***Completion of Therapy for Latent TB Infection:***

1. Below are the *minimum* number of doses required, based on regimens listed in *Table 5* and the corresponding time frame for acceptable completion of therapy.

Regimen*	Total Doses Required for LTBI Treatment Completion
INH/RPT (3HP)	**12** doses (minimum of 11 doses acceptable) administered in no fewer than 12 weeks (but no more than 16 weeks). Doses must be separated by ≥72 hours to be counted.
4 Months of Rifampin (4R)	7 days per week for **120** doses taken within 6 months, OR 5 days per week for **90** doses administered by DOT within 6 months
3 Months of INH and RIF (3HR)	7 days per week for **90** doses taken within 4 months
6 Months of Daily INH (6H)	7 days per week for **180** doses taken within 9 months, OR 5 days per week for **129** doses administered by DOT within 9 months
6 Months of Twice-Weekly INH (6H)	Twice weekly for **52** doses administered by DOT within 9 months
9 Months of Daily INH (9H)	7 days per week for **270** doses taken within 12 months, or 5 days per week for **195** doses administered by DOT within 12 months
9 Months of Twice-Weekly INH (9H)	Twice weekly for **76** doses administered by DOT within 12 months

**Refer to Table 5. Recommended Drug Regimens for Treatment of INH-and RIF-Susceptible Latent TB Infection*

2. For persons treated empirically for TB disease with at least isoniazid, rifampin, and pyrazinamide for 2 months (40 doses given by DOT 5x/week or 56 doses given by DOT 7 days/week), this regimen can be considered effective treatment of TB infection in persons subsequently determined to have infection rather than TB disease.

3. When changing treatment regimens due to adverse reactions or intolerance, the number of doses needed to complete adequate therapy must be made by the licensed health care provider.
    a. The decision to restart treatment entirely with a new regimen or counting a percentage of doses taken towards the new regimen should be made on a case-by-case basis.

b. Licensed healthcare providers should consider the patient's risk of progressing to disease, compliance, and comorbidities. Some experts recommend that certain patients complete a full course of the new regimen.
c. For others, it may not always be necessary to restart the new regimen completely to achieve completion of therapy.
d. Refer to *Section 6: Monitoring and Managing Treatment of the LTBI: Testing and Treatment of Latent Tuberculosis Infection in the United States, 3rd Edition*, for details. http://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/

ATTACHMENT 8: Patients with Drug Resistant Tuberculosis (DR-TB)

This attachment outlines required activities, procedures, and orders to be performed *in addition to* those outlined in the previous sections of these SDOs.

A. Definitions

1. Isoniazid mono-resistant TB- resistance to isoniazid, a first line TB drug.
2. Rifampin mono-resistant TB (RR)- resistance to rifampin, a first line TB drug; this type of DR-TB is treated similarly to MDR-TB.
3. Multi-drug resistant TB (MDR TB)- resistance to at least rifampin and isoniazid.
4. Pre-extensively drug resistant TB (Pre-XDR TB)- MDR, plus resistance to one of the second line injectable agents (amikacin, capreomycin, or kanamycin) *or* a fluoroquinolone.
5. Extensively drug resistant TB (XDR TB)- MDR, plus resistance to one of the second line injectable agents (amikacin, capreomycin, or kanamycin) *and* a fluoroquinolone or MDR, plus resistance to a fluoroquinolone, and Bedaquiline or Linezolid.

B. Level of Experience, Training, Competence, and Education Required

1. Have reviewed, are familiar with, and able to readily access the recommendations within the following document:
   a. Treatment of Drug-Resistant Tuberculosis, An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline (2019). Am J Respir Crit Care Med 15; 200 (10): e93-e142. https://www.atsjournals.org/doi/full/10.1164/rccm.201909-1874ST.

C. Procedures and Requirements to be Followed by Authorized Licensed Nurses Managing Patients with DR-TB

1. When resistance is identified by drug susceptibility testing (DST), rapid testing (i.e., GeneXpert NAAT), or rpoB alert, whichever comes first, or if resistance is suspected due to patient risk factors, perform the following:
   a. Contact the licensed healthcare provider.
   b. Consider holding the current regimen if not consistent with current test results and the patient is medically stable.
   c. Initiate a consultation with a DSHS-recognized TB medical consultant within three (3) working days. Do not wait for final cultures to initiate consultation, as the consultant will assist in coordination of further testing, including Molecular Detection of Drug Resistance (MDDR).
   d. Notify the TB and Hansen's Disease Unit's Nurse Consultant.

2. Respond to treatment and case management activities where indicated, unless

otherwise noted by the treating physician or consultant.

a. Drug resistance should be considered in any patient with:
   - Known exposure to an individual with drug-resistant TB
   - Residence in a setting with high rates of primary drug-resistant TB, such as a country or area with high rates of drug-resistant TB in newly diagnosed individuals
   - Persistently positive smear or culture results at or after four months of treatment
     Previous TB treatment, particularly if it was not directly observed or was interrupted for any reason

b. **Treatment:** Seven days a week of observed dosing is optimal for patients treated for drug-resistant TB. If that is not feasible, self-administration may be considered for weekend doses.
   1) Patients with BDQ included in their regimen should have a loading phase of 400mg daily for 14 days followed by a maintenance dose of 200mg three times a week for at minimum 24 weeks.
   2) Patients on BPaL or BPaLM are typically treated at minimum for 6 months (26 weeks) but in some instances, therapy may be extended to 9 months (39 weeks) based on clinical, radiographic, microbiologic evidence of delayed treatment response within the first 8 weeks.

c. **Interruptions of Therapy:** Initial and continuation phases are different for patients on treatment for DR-TB than for patients with drug-susceptible TB. Treatment interruptions should be carefully monitored by the nurse case manager, as any missed doses are concerning and may impact treatment outcomes. Consultation may be necessary when interruptions occur.
   1) Patients on BDQ may require a loading dose depending on number of doses taken and where in treatment the interruption occurs. Please refer to article: *Addressing Bedaquiline treatment interruption in the treatment of drug-resistant TB.* https://pubmed.ncbi.nlm.nih.gov/35768912/
   2) Once BDQ dosing (or linezolid if dosed three times/week) is on a three times per week schedule, missed doses are especially problematic. A single missed dose in one week is missing 33% of doses (of BDQ) which is less than the minimum tolerated 80% of doses. Even taking 80% of doses is associated with increased risk of relapse.
   3) Contact the LHP when a patient misses an observed dose.

d. **Medical screenings:** Perform the following screening assessments at the following intervals and document on the TB 702 (or equivalent). Weights should be performed at every visit or more frequently dependent on clinical assessments:

1) Baseline and monthly clinical monitoring of medication toxicity for patients on second-line medications:

- If patient is taking **aminoglycosides** (most commonly **amikacin**), this is to include:
  - audiometry screening.
  - vestibular screening.
- If patient is taking **cycloserine**, this is to include:
  - A mental health assessment to include depression screening. Also ask if they are experiencing nightmares, hallucinations, aggression or disorientation.
- If patient is taking **clofazimine**, this is to include:
  - A mental health screening to focus on depression symptoms.
- If patient is taking **linezolid**, this is to include:
  - red/green color discrimination using Ishihara plates.
  - visual acuity using Snellen chart or equivalent.
  - peripheral neuropathy screening.
- If patient is taking **high dose isoniazid (adults 15mg/kg)**, this is to include:
  - peripheral neuropathy screening.
- If patient is taking **bedaquiline (Sirturo)**, this is to include:
  - ECG at baseline, 2 weeks after initiation of treatment, and monthly. It is recommended that the licensed healthcare provider interpret the ECG within 24 hours of the ECG test.
    - Perform ECG at the designated intervals (preferably Monday-Wednesday in case further interventions such as labs or consultations are needed).
    - ECG should be performed at the same time of day each time. ECGs exhibit diurnal variation of up to +/- 75ms during the course of a day.
    - **A patient with elevated QTc intervals should have one repeat ECG done ≥ 30 minutes apart to confirm reading.**
    - Documentation of any symptoms* of prolonged QTc should be included when performing the ECG and results of both provided to the licensed healthcare provider.

Ensure the licensed healthcare provider reviews the symptoms and ECG results within 24 hours of test, unless otherwise specified, and documents response in the medical record.

- Respond to the following based on the ECG results:

If QTc is greater than 450ms (in males) or greater than 470ms (in females) and patient is ***asymptomatic**:**

- Draw CMP plus magnesium, TSH, CBC
- Contact the licensed healthcare provider to review ECG results within 24 hours
- Perform weekly ECGs until normal or until licensed healthcare provider orders otherwise

If QTc is greater than 500ms in male or females, and patient is ***asymptomatic**:**

- Hold medications
- Draw CMP plus magnesium, TSH, CBC
- Contact the licensed healthcare provider to review results within 24 hours
- Request that the licensed healthcare provider consults cardiology or a DSHS-recognized medical TB consultant
- Repeat ECG in 24-48 hours
- Perform weekly ECGs until normal or the licensed healthcare provider orders otherwise
- Do not resume regimen until instructed by the licensed healthcare provider

If QTc is greater than 450ms (in males) or greater than 470ms (in females) and patient is ***symptomatic**:**

- Refer patient to the Emergency Department (ED)- ensure there is a referral form that the patient may present to the ED already reviewed by the licensed healthcare provider which outlines at minimum: diagnosis, isolation status, current medications, baseline and current ECG results, symptoms, reason for referral to ED and TB physician contact information
- Do not resume regimen until instructed by the licensed healthcare provider

If QTc is greater than 60ms above baseline and patient is ***asymptomatic**:**

- Draw CMP plus magnesium, TSH, CBC
- Contact the licensed healthcare provider to review ECG results within 24 hours for recommendations

**Symptoms of prolonged QTc include palpitations, tachycardia, light-headedness, fainting/syncope, chest pain, loss of consciousness, shortness of breath*

Considerations for the licensed healthcare provider:
Correcting the QT interval from ECG readings: The QTc interval is influenced by the heart rate. At a HR of 60, QT = QTc using any of the formulas (Bazett, Fridericia, Framingham or Hodges). As HR increases, the QTc increases. Most ECG machines in the US use the Bazett formula which at higher HR yields a more prolonged QTc than the Fridericia formula.

It is recommended to use the Fridericia formula when calculating corrected QTc intervals as studies examining TB medications and QT prolongation used the Fridericia formula in their assessments and guidance. Consider online calculators (e.g., https://www.mdcalc.com/corrected-qt-interval-qtc) or manual calculations.

Refer to algorithms for monitoring and managing corrected QT prolongation in patients with DR-TB here: "Guide for QTc Monitoring and management of Drug-resistant TB Patients with QT Prolonging Agents" available at: https://www.challengetb.org/publications/tools/pmdt/Guidance_on_ECG_monitoring_in_NDR_v2.pdf

e. **Laboratory tests:** Patients prescribed second line medications age 18 or older will have additional labs collected under the following circumstances:
   1) At Baseline:
      - CBC and CMP.
      - A pregnancy test for females of childbearing age who are starting **clofazimine** and/or on an aminoglycoside, commonly **amikacin.**
      - For patients on **bedaquiline and amikacin**, include magnesium, which must be ordered in addition to the CMP.
      - For patients on **ethionamide**, **bedaquiline**, and **para-amino salicylic acid (PAS)**, include a TSH (thyroid stimulating hormone) level.
      - Therapeutic drug monitoring 10-14 days after treatment initiated perform the following:
        - **Linezolid (LZD)** peak and trough. Trough is done right before next dose is administered. LZD peak should be done 2 hours post dose.
        - **Moxifloxacin** peak level at 2 hours post dose.

2) Monthly:
   - CBC and CMP.
   - For patients on **bedaquiline**, include magnesium.

3) Quarterly and as needed:
   - For patients on, **ethionamide**, **PAS or bedaquiline**, include TSH.

4) As needed and/or per consultation:
   - CBC if moderate or severe anemia or other abnormalities present at baseline.
   - Therapeutic drug monitoring.

f**. <u>Radiology</u>:** Posterior-anterior (PA) view CXRs should be performed for patients over age 18; PA and lateral for patients younger than 18 and patients with HIV, in the following intervals:

1) Patients with RR/MDR/Pre-XDR/XDR pulmonary TB:
   - During treatment:
     - initially
     - at two months
     - at six months, then,
     - every six months until completion of therapy or as recommended by DSHS-recognized medical TB consultant
   - Post treatment:
     - Every six months for two years, accompanied with a TB signs and symptoms questionnaire, medical evaluation, and weight.

2) For patients who are contacts to MDR/Pre-XDR/XDR TB diagnosed with TB infection, regardless of whether they completed prophylaxis treatment for TB infection, every effort should be made to perform a TB signs and symptoms screening questionnaire and a CXR every six months for two years as this is the highest risk period for developing active disease. If symptoms of TB are present, follow up as indicated (refer to ***Attachment 5***).

g. **<u>Sputum collection</u>**: For patients with pulmonary disease, collect sputum in the following intervals after initial samples:

1) Collect at least three consecutive sputum specimens for AFB smear and culture monthly until culture conversion.

2) Continue to collect at least one sputum specimen for AFB smear and culture after culture conversion, at least once a month, until treatment completion.

3) Every effort should be made to collect at least one sputum every six months for two years after completion of therapy.

h. **Release from airborne isolation*:** It is appropriate to be more cautious when releasing these patients from airborne isolation. Contact the licensed healthcare provider for best practice. Release may be made in consultation with a DSHS-recognized medical TB consultant if needed. Considerations to release from isolation include:

- Release to a low or high-risk (i.e., congregate settings, household with small children, setting with immunocompromised individuals, and work site)
- Patient's response to therapy clinically, radiographically, and bacteriologically (some experts recommend two to three consecutive negative AFB sputum cultures prior to release from isolation.)

*Refer to:
https://www.heartlandntbc.org/wp-content/uploads/2021/12/guidelines_home_hospital_infectious_patients.pdf and
https://www.currytbcenter.ucsf.edu/sites/default/files/tb_sg3_chap8_monitoring_and_cm.pdf#infectionctrl

i. **Isoniazid mono-resistant or intolerance:** For patients with isoniazid mono-resistant TB (high or low level) or INH intolerance, the following applies:

1) Seek consultation from a DSHS-recognized medical TB consultant.

2) Ensure fluoroquinolone susceptibilities have been performed.

3) Once fluoroquinolone susceptibilities are known and no further resistance is identified, the addition of a later-generation fluoroquinolone (usually **moxifloxacin** or **levofloxacin**) may be added to the regimen.

j. **Completion of therapy:**

1) Patients with RR, MDR, Pre-XDR, or XDR TB:

- An end of treatment consult with a DSHS-recognized TB medical expert is required prior to stopping treatment.
- Determine completion of therapy based on total number of observed doses administered, clinical, radiological, and bacteriological improvement.

ATTACHMENT 9: Medical Consultation Indications

Consultation is required or recommended in the situations described below. Options for medical consultation include DSHS Recognized TB Medical Consultants or a DSHS Regional Medical Director.

Contact information for DSHS-Recognized TB Medical Consultants may be found at: http://www.dshs.texas.gov/idcu/disease/tb/consultants/

Contact information for DSHS Regional Medical Directors may be found at: https://www.dshs.texas.gov/regional-local-health-operations/public-health-regions

Consultation REQUIRED when:

1. Patient is a contact to a case of RR, MDR, Pre-XDR, or XDR TB.
2. Patient has laboratory-confirmed drug resistance or is suspected to have drug resistant-TB.
    - Laboratory-confirmed drug resistance is defined as resistance to isoniazid and/or rifampin, or to any drug other than streptomycin* on drug susceptibility panel testing.
    - Consultation must occur within 3 days of laboratory notification.

    **If the organism is identified as M. bovis with PZA monoresistance, consult is not required.*
3. Patient with RR, MDR, Pre-XDR, or XDR TB is reaching end of treatment and prior to stopping treatment.
4. When isoniazid or a rifamycin cannot be used due to intolerance or drug-interactions in a regimen for active TB.
5. Patient has positive sputum cultures for *M.tb* after 4 months of appropriate therapy for TB disease and is deemed a treatment failure.
6. Patient has been prescribed a second line medication.
7. Patient has been prescribed a regimen for TB disease that is less than daily dosing.

Consultation RECOMMENDED when:

1. Patient has HIV infection and is on or anticipates starting on antiretrovirals.
2. Patient has complex medical comorbidities.
3. Patient has serious forms of tuberculosis, e.g., disseminated or meningeal TB.
4. Patient is under the age of 5 years.
5. Patient's symptoms or CXR have not improved after the first 2 months of treatment.
6. Patient has a positive sputum smear for acid-fast bacilli and/or positive sputum culture for *M.tb* after 2 months of appropriate therapy for TB disease.
7. When therapeutic drug monitoring is being considered, and the patient is not clinically, radiographically, or bacteriologically improving after 2 months of

appropriate therapy for TB disease.

8. Patient has treatment interrupted for more than 2 weeks in the initial phase of therapy for TB disease.
9. Patient has treatment interrupted for more than 3 months in the continuation phase of therapy for TB disease.
10. Patient has completed treatment for MTB and is recommended therapy again within a 12-month period for recurrence of signs or symptoms.