

TUBERCULOSIS TECHNICAL INSTRUCTIONS FOR



# PANEL PHYSICIANS

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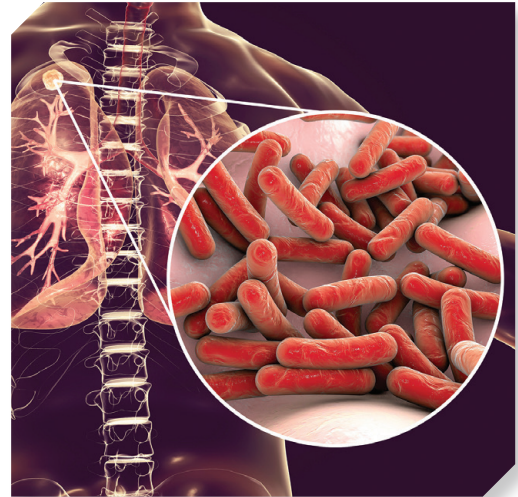


**Centers for Disease  
Control and Prevention**  
Division of Global Migration  
and Quarantine



## OVERVIEW OF TUBERCULOSIS TECHNICAL INSTRUCTIONS

The medical screening for tuberculosis among persons overseas applying for US immigration status and nonimmigrants who are required to have an overseas medical examination, hereafter referred to as applicants, is an essential component of the medical evaluation. Because tuberculosis is a challenging disease to diagnose, treat, and control, these instructions are designed to enable panel physicians overseas to detect and treat infectious forms of tuberculosis among applicants and to reduce the risk of spread of tuberculosis among the US population after immigration.

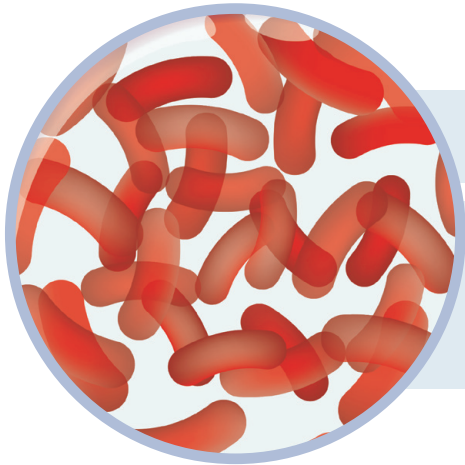


Pulmonary tuberculosis is a disease that involves the lung parenchyma and is often infectious (i.e., contagious [determined by sputum smear examination for acid-fast bacilli (AFB) and mycobacterial culture]). Laryngeal tuberculosis is rare but highly infectious. Disease of the lung parenchyma may occur concurrently with pleural tuberculosis, and the parenchymal lung disease may not be apparent on chest radiograph because of compression of affected lung tissue by pleural fluid. Because the emphasis for the pre-immigration medical evaluation is on infectiousness, for the purpose of this document, the term [tuberculosis disease](#) refers to disease of the lung parenchyma, pleural tuberculosis, laryngeal tuberculosis, and tuberculosis of the intrathoracic lymph nodes. Other forms of [extrapulmonary tuberculosis](#) and [latent tuberculosis infection](#) (LTBI) are not included in the definition of tuberculosis disease for the purposes of these Technical Instructions and are defined separately.

The Division of Global Migration and Quarantine (DGMQ) developed these instructions in consultation with US tuberculosis subject matter experts and US panel physicians. These instructions define the specific responsibilities of panel physicians in terms of testing and treatment of tuberculosis disease among applicants overseas for purposes of US immigration medical eligibility only. These instructions are specific to the immigration medical evaluation and should not be used as guidelines to test for or treat tuberculosis disease in other settings or as a clinical manual that defines detailed laboratory procedures or specific treatment regimen details. Drug-susceptible tuberculosis disease treatment of applicants must be consistent with the current [Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis](#).

The instructions in this document supersede all previous Tuberculosis Technical Instructions, Updates to the Technical Instructions, memoranda and letters to panel physicians, and memoranda and letters to international refugee resettlement organizations. These instructions are to be followed for tuberculosis disease screening and treatment of all applicants.





## TUBERCULOSIS SCREENING

**Applicants in all countries who are  $\geq 15$  years old must have chest radiography (chest x-ray).**

**Applicants 2 through 14 years old living in countries with a World Health Organization (WHO)-estimated tuberculosis incidence rate of  $\geq 20$  cases per 100,000 population must have an IGRA.**

A complete screening medical examination for tuberculosis disease consists of a medical history, physical examination, IGRA when required, chest x-ray when required, and sputum smears and culture testing for *Mycobacterium tuberculosis* (when required, Figures 1a.,b. and 2a.,b.). Requirements vary based on age of applicant and the WHO-estimated tuberculosis disease incidence rate in the country where the exam occurs.

HIV testing is no longer part of the U.S. medical screening process, however, panel physicians may advise applicants about HIV testing for whom testing is clinically indicated. Such applicants may include those with signs and symptoms suggestive of HIV infection or those with tuberculosis disease. For such applicants, the consent for HIV testing should include the following:

- Applicants understand they do not have to be tested for HIV.
- Applicants understand that if they would like to be tested for HIV, they do not have to be tested for HIV by a panel physician.
- Applicants understand that panel physicians must include the test results on the paperwork they complete.

If applicants who would benefit from HIV testing provide consent, panel physicians should perform HIV testing consistent with the standards of testing in their countries.

People with HIV infection are less likely to have an abnormal chest x-ray during tuberculosis disease; and negative IGRA results do not rule out tuberculosis disease, thus all applicants with known HIV infection must provide sputum specimens for microscopy and culture regardless of IGRA and chest x-ray results in order to rule out tuberculosis disease.

## Tuberculosis screening for applicants in countries with a WHO-estimated tuberculosis disease incidence rate of <20 cases per 100,000 population

All applicants <15 years of age living in countries with a WHO-estimated tuberculosis disease incidence rate of <20 cases per 100,000 population must have a physical examination and history provided by a parent or responsible adult who knows the child best (Figure 1a.). Those applicants who have signs or symptoms suggestive of tuberculosis disease or have known human immunodeficiency virus (HIV) infection must have an IGRA and a chest x-ray (anteroposterior or posteroanterior view and a lateral view for applicants <10 years of age; posteroanterior view for applicants ≥10 years of age), and provide three sputum specimens to undergo microscopy for AFB, as well as culture for mycobacteria, confirmation of the *Mycobacterium* species at least to the *M. tuberculosis* complex level, and drug susceptibility testing for positive cultures.

Applicants ≥15 years of age living in countries with a WHO-estimated tuberculosis disease incidence rate of <20 cases per 100,000 population must have a medical history, physical examination, and chest x-ray (Figure 1b.). Those applicants who have signs or symptoms suggestive of tuberculosis disease, chest x-ray findings suggestive of tuberculosis disease, or known HIV infection must provide three sputum specimens to undergo microscopy for AFB, as well as culture for mycobacteria, confirmation of the *Mycobacterium* species at least to the *M. tuberculosis* complex level, and drug susceptibility testing for positive cultures.

## Tuberculosis screening for applicants in countries with a WHO-estimated tuberculosis disease incidence rate of ≥20 cases per 100,000 population

All applicants <2 years of age living in countries with a WHO-estimated tuberculosis disease incidence rate of ≥20 cases per 100,000 population must have a physical examination and history provided by a parent or responsible adult who knows the child best. Applicants who have signs or symptoms suggestive of tuberculosis disease or have known HIV must have an IGRA or tuberculin skin test (TST) and a chest x-ray (anteroposterior or posteroanterior view and a lateral view), and must provide three sputum specimens to undergo microscopy for AFB, as well as culture for mycobacteria, confirmation of the *Mycobacterium* species at least to the *M. tuberculosis* complex level, and drug susceptibility testing for positive cultures.

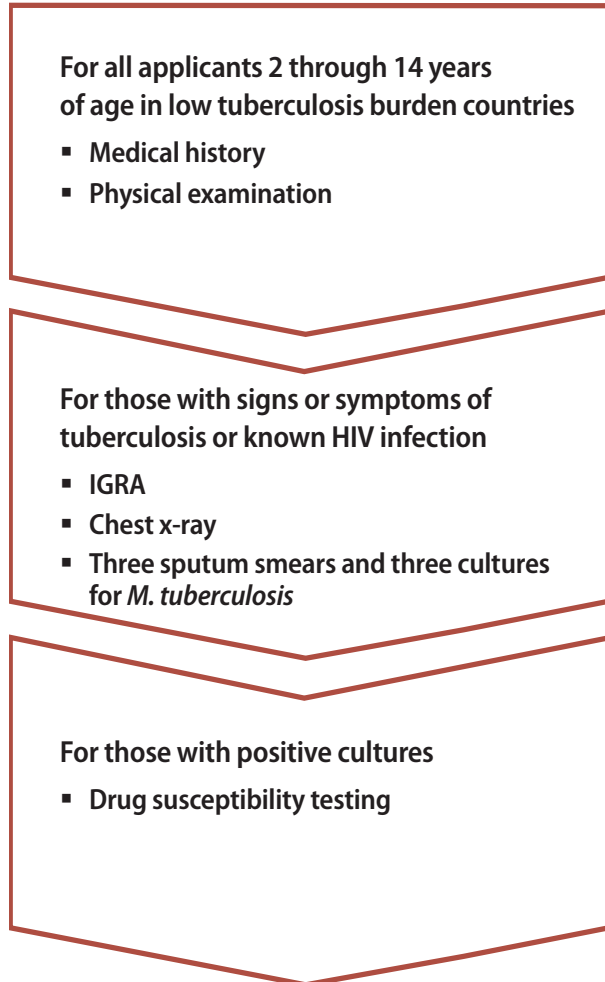
IGRA testing is required for all applicants 2 through 14 years old who are living in countries with a WHO-estimated tuberculosis disease incidence rate of ≥20 cases per 100,000 population (Figures 2a.). IGRA must be performed for these applicants if a US Food and Drug Administration (FDA)-approved IGRA test is licensed for use in the country in which the panel physician is practicing. If IGRA is not licensed for use in the country, TST should be used for these applicants. [Current US clinical practice guidelines](#) suggest using TST rather than an IGRA in healthy children <5 years of age; some pediatric experts use IGRA for younger children ([Red Book 2018](#)). Because of programmatic concerns in the setting of this examination, panel physicians must use an IGRA as defined in these instructions for all applicants 2 years through 14 years of age.

For applicants 2 through 14 years of age living in countries with a World Health Organization (WHO) estimated tuberculosis disease incidence rate of ≥20 cases per 100,000 population, if the IGRA is positive or if the applicant has signs or symptoms of tuberculosis disease or has known HIV infection, a chest x-ray (anteroposterior or posteroanterior view and a lateral view for applicants <10 years of age; posteroanterior view for applicants ≥10 years of age) must be performed. Applicants who have a chest x-ray with findings suggestive of tuberculosis disease, signs or symptoms of tuberculosis disease, or known HIV infection must provide three sputum specimens to undergo microscopy for AFB, as well as culture for mycobacteria, confirmation of the *Mycobacterium* species at least to the *M. tuberculosis* complex level, and drug susceptibility testing for positive cultures.

Applicants ≥15 years of age who are living in countries with a WHO-estimated tuberculosis disease incidence rate of ≥20 cases per 100,000 population must have a chest x-ray (Figure 2b.). If an applicant has a chest x-ray with findings suggestive of tuberculosis disease, has signs or symptoms of tuberculosis disease, or has known HIV infection, the applicant must provide three sputum specimens to undergo microscopy for AFB, as well as culture for mycobacteria, confirmation of the *Mycobacterium* species at least to the *M. tuberculosis* complex level, and drug susceptibility testing for positive cultures.

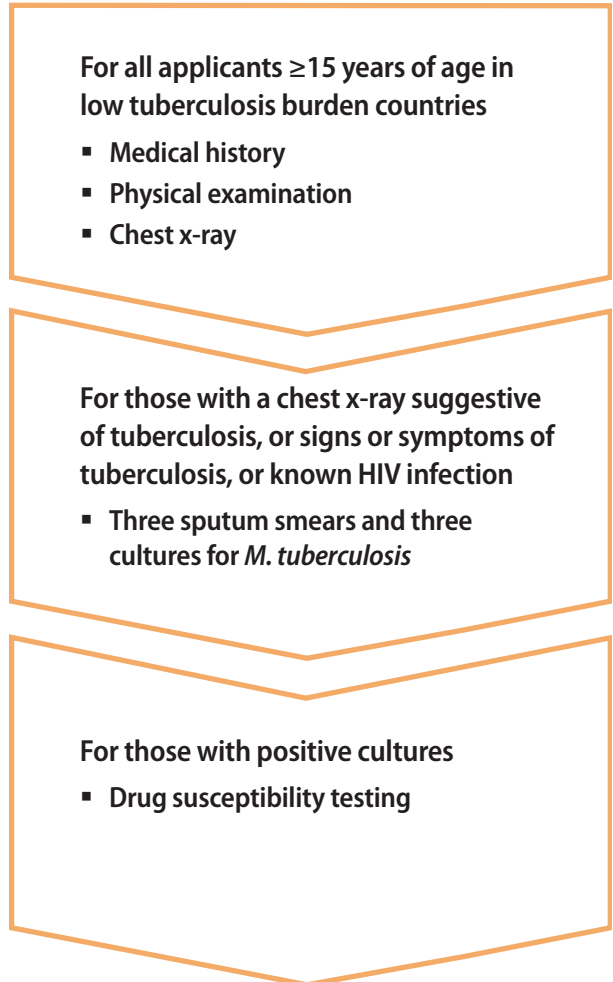


**Figure 1a:** Tuberculosis screening for applicants 2 - 14 years of age in low TB burden countries\*



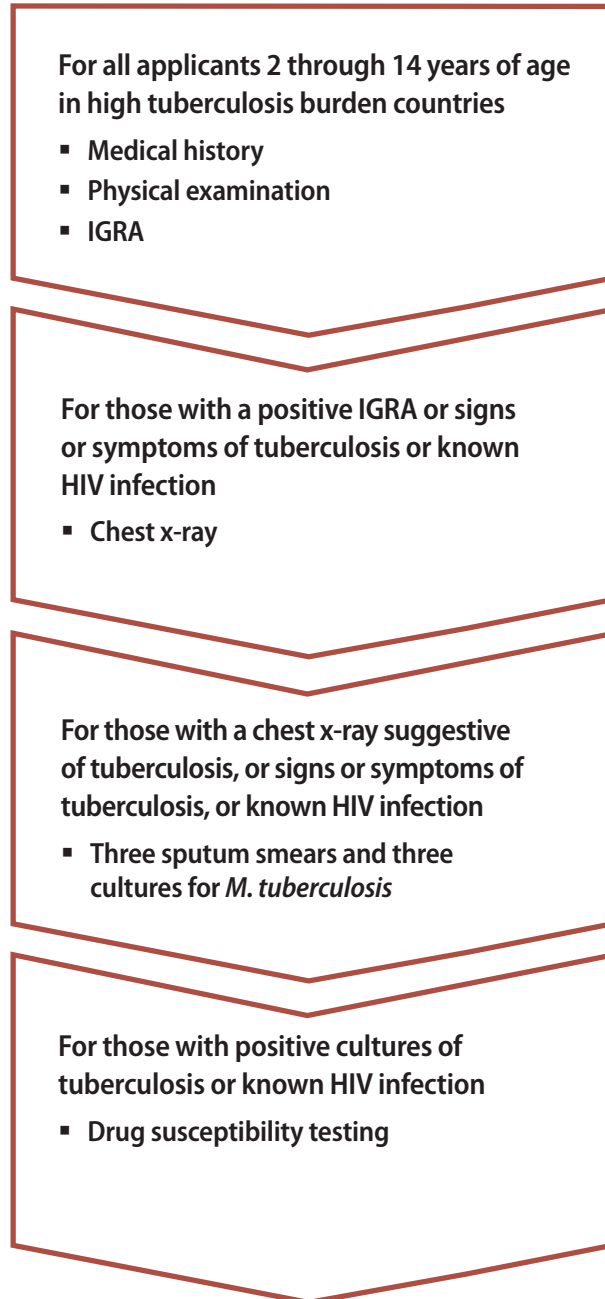
\*Tuberculosis screening for applicants 2 through 14 years of age in countries with a WHO-estimated tuberculosis disease incidence rate <20 cases per 100,000 population.

**Figure 1b:** Tuberculosis screening for applicants 15 years of age or older in low TB burden countries\*



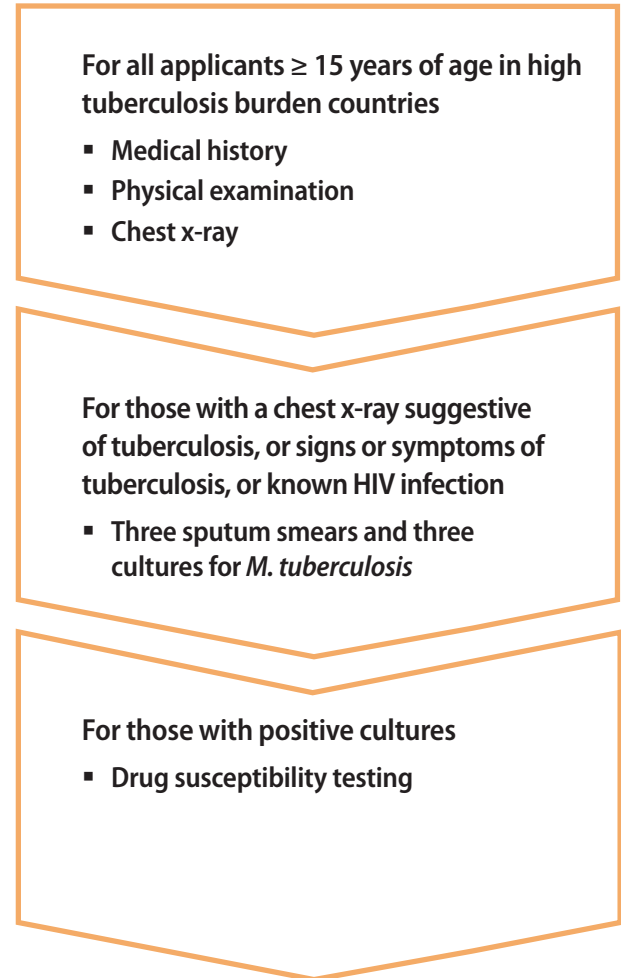
\*Tuberculosis screening for applicants ≥15 years of age in countries with a WHO-estimated tuberculosis disease incidence rate <20 cases per 100,000 population.

**Figure 2a:** Tuberculosis screening for applicants 2 - 14 years of age in high TB burden countries\*



\*Tuberculosis screening for applicants 2 through 14 years of age in countries with a WHO-estimated tuberculosis disease incidence rate  $\geq 20$  cases per 100,000 population.

**Figure 2b:** Tuberculosis screening for applicants 15 years of age or older in high TB burden countries\*



\*Tuberculosis screening for applicants  $\geq 15$  years of age in countries with a WHO-estimated tuberculosis disease incidence rate  $\geq 20$  cases per 100,000 population.

## Each aspect of the examination for tuberculosis is detailed below.

### Medical History

- The medical history should focus on risk factors for tuberculosis disease, including previous history of tuberculosis disease; illness suggestive of tuberculosis disease (such as cough of >3 weeks' duration, dyspnea, weight loss, fever, or hemoptysis); prior treatment suggestive of tuberculosis disease treatment; and prior diagnostic evaluation suggestive of tuberculosis disease. The clinical expression of tuberculosis disease may be different in children than in adults, and for children may only include generalized findings such as fever, night sweats, growth delay, and weight loss. Children are also more prone to extrapulmonary tuberculosis, such as meningitis, and disease of the middle ear and mastoid, lymph nodes, bones, joints, and skin.
- The medical history should also include inquiries regarding family or household contact with a person who has or had tuberculosis disease, or an illness, treatment, or diagnostic evaluation suggestive of tuberculosis disease.
- Prior receipt of bacille Calmette-Guérin (BCG) vaccination should be ascertained; review and record if documentation and date of receipt are available. Many applicants may have previously received BCG vaccination. Prior receipt of BCG does not change the screening requirements or the required actions based on those results.
- Applicants with a remote history of tuberculosis disease who have a normal chest x-ray, no current signs or symptoms of tuberculosis disease, and no known HIV infection should be assigned "No TB Classification".

### Physical Exam

- Pertinent elements of the physical exam for tuberculosis disease include general characteristics such as height, weight, temperature, heart rate, respiratory rate, and blood pressure; a thorough pulmonary examination; inspection and palpation of lymph nodes; and inspection for scars of scrofula and prior chest surgery.

### Immune Response to *M. tuberculosis* Antigens

Applicants 2 through 14 years of age living in countries with a WHO-estimated tuberculosis disease incidence rate of  $\geq 20$  cases per 100,000 population must have an IGRA test to determine immune response to *M. tuberculosis* antigens.

Exceptions include applicants with written documentation from a physician of a previous positive IGRA. Applicants 2 through 14 years of age living in countries with a WHO-estimated tuberculosis disease rate of  $\geq 20$  per 100,000 who provide documentation of a previous positive TST must still have an IGRA performed; if the IGRA is negative, the applicant is considered to have a negative immune response to *M. tuberculosis* antigens in this examination. For past positive IGRA results, the written documentation must include date of the test, type of IGRA performed, test results in standard units of measurement, the test interpretation (e.g., positive, negative, indeterminate, borderline), and the testing physician's name, signature, and office information. Applicants 2 through 14 years of age with a documented previous history of tuberculosis disease must have a chest x-ray, even if their IGRA is negative.

- Interferon Gamma Release Assays (IGRA)  
Interferon gamma release assays are blood tests that measure a component of cell-mediated immune reactivity to *M. tuberculosis*. CDC will only allow use of IGRA tests approved by the US Food and Drug Administration (FDA). Currently, the FDA-approved options are QIAGEN QuantiFERON® (any iteration approved by FDA) or Oxford Immunotec T-SPOT®.TB. Panel physicians must follow the manufacturers' written instructions for collecting samples, performing tests, and interpreting test results. For the purpose of tuberculosis screening according to these Technical Instructions, an indeterminate test result must be documented as indeterminate and not result in repeat testing by the panel physician, chest x-ray, or B2 classification. However, applicants with an indeterminate test result should be advised to have a repeat test after arrival to the United States. IGRA results should be available within 48 hours of sample collection.





- Tuberculin Skin Test (TST)

TST can only be used as a substitute for IGRA when an FDA-approved IGRA product is not licensed for use by the country in which the panel physician practices, or in children under 2 years of age when indicated. PPD must be administered intradermally by the Mantoux method. Ideally, preparations used should be equivalent to 5TU PPD-S. However, in countries where such preparations are limited or impossible to import, panel physicians must use PPD preparations that are approved for use by their ministries of health. The type of PPD used must be documented. A TST is considered positive if it is  $\geq 10$  mm ( $\geq 5$  mm if applicant is a known contact to a recent case of tuberculosis disease).

## CHEST RADIOGRAPHY

When performed, chest radiography (chest x-ray) must consist of a standard posteroanterior view for all applicants  $\geq 10$  years of age. Applicants  $< 10$  years of age who receive a chest x-ray should have a standard anteroposterior or standard posteroanterior view and must also have a lateral view. If a child  $< 10$  years of age undergoes a posteroanterior view, the chest x-ray should be labeled "PA" for the benefit of the radiologist's review.

Chest x-rays must be interpreted by a radiologist and reviewed by the panel physician. The radiologist who interprets the image must complete and sign the radiology portion of the US Department of State (DS) form or eMedical application. Chest x-ray results must be available within 1 week from the time they were performed. An applicant's chest x-ray should be retaken if the initial chest x-ray is suboptimal because of factors such as motion artifact or low lung volumes. Chest x-ray interpretations should include comparisons with prior chest x-rays, if available.

Applicants with clinical and radiographic findings suggestive of common bacterial infections of the respiratory tract may be treated with a course of antibiotics. However, fluoroquinolones should not be used for empiric treatment of respiratory infections because they are a mainstay of second-line therapy for tuberculosis disease and their use could both result in mistreatment of tuberculosis disease and lead to drug-resistant tuberculosis disease. The chest x-ray for medical screening should not be performed until at least 8 weeks after treatment for respiratory tract infections unless the applicant's clinical status warrants further evaluation earlier than 8 weeks after therapy.

Women who are pregnant may postpone the required immigration chest x-ray (and immigration medical examination) until after pregnancy but are required to have a chest x-ray to immigrate. Panel physicians must obtain consent from pregnant women before performing a chest x-ray. Panel physicians should develop their own consent form for this scenario. Pregnant women undergoing chest x-ray must be provided abdominal and pelvic protection with two lead shields that wrap fully around the abdomen and pelvis.

The panel sites must use digital radiography (computed radiography (CR) or direct digital radiography (DDR)) to obtain plain chest radiographs for applicants. Digitized analog images are not digital images and are not acceptable.

Digital radiography equipment systems and interpretations must meet the following requirements:

- Images must be interpreted by a radiologist on a high-resolution screen. The screens must be medical-grade monitors that are at least 3 megapixels (MP) in "display resolution" AND that are advertised as being appropriate for primary image interpretation (not for image review). The screens used by the panel physicians to review the images are not required to meet this standard.
- Images may not be interpreted from laser-printed films, as the quality of printing varies greatly and film format cannot be optimized.

## SPUTUM COLLECTION

- Laboratory examination for tuberculosis disease must consist of at least three sputum specimens. Each specimen must undergo microscopy for AFB as well as culture for mycobacteria, confirmation of the *Mycobacterium* species, at least to the *M. tuberculosis* complex level, and drug susceptibility testing for positive cultures.
- Once the panel physician notifies the applicant that sputum specimens are required, the applicant must report for testing as soon as possible. If testing is delayed longer than 2 weeks, the panel physician should strongly consider testing the applicant for the presence of tuberculosis disease treatment medications.
- The sputum specimen must be an early morning fasting specimen, and collection must be directly observed by a health-care provider. Applicants should be instructed not to brush their teeth or use mouth wash prior to sputum collection. Three specimens consisting of 5–10 mL each must be collected at least 24 hours apart, preferably on consecutive working days. Applicants must rinse their mouths with purified or distilled water before providing a sputum specimen.
- Salivary specimens are unacceptable. The collection of a true sputum specimen is of critical importance to rule out tuberculosis disease, and the person collecting sputum must ensure it is not a salivary specimen before sending it to the laboratory.
- Applicants unable to produce sputum specimens, such as young children, are required to have alternative methods of sputum collection performed (e.g., early morning gastric aspirates or sputum induction or both) to determine their tuberculosis disease status.
- For applicants who have difficulty producing sputum, there are several methods of obtaining a specimen. Inhalation of an aerosol of sterile hypertonic saline (3%–5%), usually produced by an ultrasonic nebulizer, can be used to stimulate the production of sputum (sputum induction). Even though aerosol-induced specimens may appear thin and watery, they should be processed. The specimen must be clearly labeled as “induced sputum” so it will not be discarded by the laboratory as an inadequate (salivary) specimen. Sputum induction can be used for children as young as 3 years of age.
- A gastric aspirate specimen can be used for all ages (but sputum is preferable in older children and adults) and may be especially helpful in young children. Three specimens must be collected, preferably on consecutive days. Detailed gastric aspirate guidance is published by the [Curry International Tuberculosis Center](#).
- If an adult is unable to provide sputum, flexible bronchoscopy is acceptable for obtaining a specimen. If bronchoscopy is used, only one procedure is required. During the bronchoscopy, two specimens must be obtained from different areas of the lung. These specimens must then be sent to the laboratory for sputum smear and culture.
- Specimens must be transported to the laboratory promptly. If not transported within 1 hour, specimens must be refrigerated (but not frozen). Specimens received in the laboratory must be processed within 24 hours of receipt. Sputum specimens must undergo centrifugation before smears are performed.

## TUBERCULOSIS CULTURE AND DRUG SUSCEPTIBILITY TESTING

All sputum specimens must be cultured for mycobacteria and confirmation of the *Mycobacterium* species, at least to the *M. tuberculosis* complex level. Solid and liquid cultures must be performed. Specimens reported as negative must be cultured for a minimum of 6 weeks for liquid cultures and 8 weeks for solid cultures, with a final report produced within 8 weeks of collection. Positive cultures must be reported as soon as the results are known.

- Positive *M. tuberculosis* cultures must undergo drug susceptibility testing (DST) for isoniazid, rifampin, ethambutol, pyrazinamide, and streptomycin. Panel physicians must have access to DST results within 10 weeks of sputum collection.
- Positive *M. tuberculosis* cultures that are resistant to rifampin (either rifampin mono-resistance or with isoniazid) must undergo drug susceptibility testing on second-line tuberculosis disease medications. At a minimum, second-line testing must include testing for resistance against ethionamide, a fluoroquinolone (e.g., ofloxacin, levofloxacin, moxifloxacin), amikacin, capreomycin, and para-aminosalicylic acid (PAS).



- The laboratory requirements in these instructions do not prevent panel physicians from using additional molecular tests for tuberculosis disease that they may have access to, such as the Hain GenoType® MTBDRplus assay or Cepheid Xpert® MTB/RIF or Xpert® MTB/RIF Ultra (Ultra). These tests might be particularly helpful when there is a strong suspicion of drug resistance or in areas where non-tuberculous mycobacteria (NTM) contamination is common. Panel physicians can only use tests that have regulatory approval in the country in which they would be used, and only use the tests for the purposes for which they have been approved. Panel physicians may base treatment decisions on the results of regulatory-approved tests for tuberculosis disease. Molecular testing can augment the use of AFB smears and cultures but cannot be used to replace AFB smears or cultures to clear applicants for travel.

In addition to these requirements provided, panel physicians should use their clinical judgment in the evaluation and diagnosis of tuberculosis disease.



## TUBERCULOSIS CLASSIFICATIONS AND TRAVEL CLEARANCE

Any applicant diagnosed with tuberculosis disease who needs treatment must receive a classification of Class A TB and is not cleared for travel until successful treatment, regardless of the diagnostic criteria.

Applicants must be assigned one or more tuberculosis classifications on the DS forms.

### The tuberculosis classifications and travel clearance times are listed below.

#### No TB Classification

Applicants without current clinical findings of tuberculosis disease, without known HIV infection, and with a normal chest x-ray (and for applicants who require it, a negative IGRA) with normal tuberculosis disease screening examinations. Travel clearance is valid for 6 months from the time the evaluation is complete.

#### Class A TB Disease

All applicants who have tuberculosis disease. This also includes applicants with extrapulmonary tuberculosis who have a chest x-ray suggestive of pulmonary tuberculosis disease, regardless of sputum smear and culture results. These applicants are not cleared for travel until completion of treatment unless a waiver is granted.

#### Class B0 TB, Pulmonary

Applicants who were diagnosed with tuberculosis by the panel physician or presented to the panel physician while on tuberculosis treatment and successfully completed DGMQ-defined [DOT](#) under the supervision of a panel physician prior to immigration. Travel clearance is valid for 3 months from the date final cultures are reported as negative. Document this classification in the remarks section of the DS form until the DS forms can be updated to include B0.

#### Class B1 TB, Pulmonary

Applicants who have signs or symptoms, physical exam, or chest x-ray findings suggestive of tuberculosis disease, or have known HIV infection, but have negative AFB sputum smears and cultures and are not diagnosed with tuberculosis disease. This classification also includes applicants who were diagnosed with tuberculosis disease by the panel physician, refused DOT treatment, and are returning after treatment and completion of 1-year wait. If all parts of the examination are complete, travel clearance is valid for 3 months from the date final cultures are reported as negative.



### **Class B1 TB, Extrapulmonary**

Applicants diagnosed with extrapulmonary tuberculosis with a normal chest x-ray and negative sputum smears and cultures. Travel clearance is valid for 3 months from the date final cultures are reported as negative.

### **Class B2 TB, LTBI Evaluation**

Applicants who have a positive IGRA or TST but otherwise have a negative evaluation for tuberculosis. The IGRA result or size of the TST reaction, the applicant's status with respect to LTBI treatment, and the medication(s) used must be documented. For applicants who had more than one IGRA or TST, all dates and results and whether the applicant's IGRA or TST converted must be documented. Contacts with a positive IGRA or TST  $\geq 5$  mm must receive this classification in addition to a Class B3, Contact Evaluation classification (if they are not already Class B0 TB, Pulmonary, B1 TB, Pulmonary, B1 TB, Extrapulmonary, or Class A TB). Travel clearance is valid for 6 months from the time the evaluation is complete.

### **Class B3 TB, Contact Evaluation**

Applicants who are a recent contact of a known tuberculosis disease case, regardless of IGRA or TST results. The IGRA result or the size of the applicant's TST reaction must be documented. If the IGRA or TST is positive and there is no evidence of tuberculosis disease, there will be two classifications, B2 and B3; if negative, B3 only. Information about the source case, name, alien number (if applicable), relationship to contact, and drug resistance of tuberculosis disease must also be documented. Additional information can be found in the [Contacts of Tuberculosis Cases](#) section. Travel clearance is valid for 6 months from the time the evaluation is complete.

### **TB Classification Pending**

Applicants with signs or symptoms suggestive of tuberculosis disease, a chest x-ray suggestive of tuberculosis disease, or known HIV infection must have three sputum specimens to undergo microscopy for AFB, as well as culture for mycobacteria, confirmation of the Mycobacterium species at least to the *M. tuberculosis* complex level, and drug susceptibility testing for positive cultures. Any laboratory or additional studies deemed necessary, either as a result of the physical examination or pertinent information elicited from the applicant's medical history, must be performed to reach a conclusion about the presence or absence of tuberculosis disease.

### **Additional Information about TB Classifications and Travel Clearance**

- Applicants can be both Class B1 and Class B3, or Class B2 and Class B3. However, other combinations of tuberculosis classifications are not permitted.
- Applicants who have sputum smears that are positive for AFB microscopy cannot be cleared for travel and should be started on treatment for tuberculosis disease (Class A TB). If panel physicians have access to molecular tests, and if molecular testing on smear-positive specimens is negative, panel physicians may wait to start treatment until culture results are reported if, in their clinical judgment, the applicant may not have tuberculosis disease. If the cultures are subsequently negative, panel physicians should use their clinical judgment to determine whether continued treatment for tuberculosis disease is warranted. If the decision is made that the applicant does not have tuberculosis disease, treatment may be stopped and the applicant may be given a Class B1 TB, Pulmonary classification.
- If the culture results are negative or demonstrate nontuberculous mycobacteria (NTM), panel physicians should use their clinical judgment in determining whether to continue treatment for tuberculosis disease. If applicants have NTM and the panel physician does not feel further treatment for tuberculosis disease is warranted, those applicants may be cleared for travel. NTM is not the same as tuberculosis disease as defined in these Technical Instructions and is not a Class A condition. In areas with high levels of NTM, an applicant may have a positive sputum smear but a negative molecular test if the positive AFB smear is from an NTM organism. In that scenario, panel physicians may use their clinical judgment to determine whether to start treatment for tuberculosis disease. The presence of NTM must be documented on the DS forms. Applicants who had an abnormal chest x-ray or signs or symptoms suggestive of tuberculosis disease, or known HIV infection, must be assigned a Class B1 TB, Pulmonary classification.

- Applicants who have negative sputum smears and positive *M. tuberculosis* cultures may not be cleared for travel and must be treated for tuberculosis disease (Class A TB).
- Applicants diagnosed with extrapulmonary tuberculosis only (except for laryngeal or pleural tuberculosis, or tuberculosis of the intrathoracic lymph nodes or lung parenchyma) must have a chest x-ray and must provide three sputum specimens to undergo microscopy for AFB and culture for mycobacterium, regardless of chest x-ray results. If the chest x-ray is suggestive of pulmonary tuberculosis disease, they are Class A TB and must complete [directly observed therapy \(DOT\)](#) as defined by the Division of Global Migration and Quarantine (DGMQ) in these Technical Instructions even if sputum smears and cultures are negative. If the chest x-ray is normal, and the sputum smears and cultures are negative, these applicants can be cleared for travel and assigned a Class B1 TB, Extrapulmonary tuberculosis classification. Applicants with extrapulmonary tuberculosis, normal chest x-ray, and negative sputum smears and cultures should be considered for treatment if departure is not planned within 3 months or if withholding therapy would be harmful. These applicants should receive DGMQ-defined [DOT](#) and be instructed on the importance of completing therapy after their arrival in the United States. They must be given a 30-day supply of medication at departure.
- Applicants who have negative sputum smears and cultures but have one of the cultures reported as “contaminated” may still be cleared for travel. When applicants have 2 or more contaminated cultures, panel sites and their designated laboratories should review their procedures and collect three additional sputum specimens from the applicant for AFB microscopy and culture.
- Applicants who have been diagnosed with tuberculosis disease by panel physicians and who do not receive DGMQ-defined [DOT](#) are not cleared for travel. These applicants will need to repeat their medical screening examination 1 year after treatment is completed. If the tuberculosis disease examination is negative at that time, the applicant can be cleared for travel. The applicant must receive a Class B1 TB, Pulmonary classification. See the “[Tuberculosis Treatment](#)” section of this document for additional information.
- Applicants with Class A tuberculosis disease who complete DGMQ-defined [DOT](#), have a negative chest x-ray, and have no signs or symptoms of tuberculosis disease, must receive a Class B0 TB, Pulmonary classification. If they do not depart and must be re-examined a year or more after treatment has ended, their new chest x-ray is negative, they have no signs or symptoms of tuberculosis disease, and have no known HIV infection, they must then be given No TB Classification.
- Applicants 10 years of age or younger who require sputum cultures, regardless of HIV infection status, may travel to the United States immediately after sputum smear analysis results are reported as negative (while culture results are pending) if none of the following three conditions exist:



1. Chest radiograph findings include:
    - ◆ One or more cavities
    - ◆ Extensive disease (e.g., particularly if involving both upper lobes)
  2. Respiratory symptoms include a forceful and productive cough
  3. Known contact with a person with multidrug-resistant tuberculosis disease (MDR TB) who was infectious at the time of contact
- For applicants 10 years of age or younger who travel to the United States while results of cultures are pending, the panel physicians must:
- ◆ Give the applicant a Class B1 TB, Pulmonary classification.
  - ◆ Document on the Tuberculosis Worksheet (DS 3030) that culture results are pending.
  - ◆ E-mail culture results to DGMQ at [cdcQAP@cdc.gov](mailto:cdcQAP@cdc.gov) so that DGMQ can send the culture results to the receiving US health departments.

For applicants 10 years of age and younger, panel physicians must provide the DS forms at the time of intended travel. If the child will not travel until after culture results are reported, panel physicians must wait to complete the DS forms until results are available. If the child will travel while results of cultures are pending, the panel physician must enter “pending” in the “Date specimen reported” field of the medical exam form and provide DS forms while cultures are pending.



## TUBERCULOSIS TREATMENT

[Directly observed therapy \(DOT\)](#) is an adherence-enhancing strategy in which a health-care worker watches a patient swallow each dose of medication in person.

Medication regimens for drug-susceptible tuberculosis must be consistent with the current ATS/CDC/IDSA guidelines ([Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis](#)).

Use only quality-assured drugs. Consult the World Health Organization (WHO) Global Drug Facility (GDF) for first-line drugs and the International Dispensary Association (IDA, Amsterdam) or WHO Green Light Committee for second-line drugs.

Panel physicians must provide [DOT](#) treatment to applicants or identify in-country treatment programs that follow the [DOT](#) standards defined in these Technical Instructions by DGMQ. Treatment provided outside the panel physician clinic must be evaluated in advance and closely supervised by the panel physician to ensure compliance with the Technical Instructions.

Treatment of tuberculosis disease must be administered following DGMQ-defined [DOT](#) policies and practices during the entire course of therapy. [DOT](#) is an adherence-enhancing strategy in which a health-care worker watches a person swallow each dose of medication in person and documents the dose. Directly observed therapy is the standard of care for all applicants with tuberculosis disease.

The panel physician has an ethical obligation to make good-faith efforts to treat patients. Applicants diagnosed with tuberculosis disease, regardless of laboratory and clinical criteria for the diagnosis, who do not want to be treated may not travel to the United States. Panel physicians must notify the Consulate of any Class A applicants refusing DGMQ-defined [DOT](#) tuberculosis disease treatment. Panel physicians must notify the appropriate public health officials in their jurisdiction when they diagnose applicants with tuberculosis disease, and if efforts to treat them fail.

Treatment of US applicants must be consistent with the current [official American Thoracic Society \(ATS\)/CDC/Infectious Diseases Society of America \(IDSA\) clinical practice guidelines](#) for treatment of drug-susceptible tuberculosis disease, including being guided by drug-susceptibility testing results. Sites may not substitute local treatment standards for ATS/CDC/IDSA standards for these applicants.

Identification of an applicant with rifampin resistance (mono-resistance, multidrug-resistant tuberculosis disease [MDR], or extensively drug-resistant [XDR] TB) must be reported to DGMQ ([cdcQAP@cdc.gov](mailto:cdcQAP@cdc.gov)) within 1 week of receipt of the DST report.

Treatment of rifampin-resistant disease must be done in close consultation with experts in the management of such cases and in coordination with DGMQ. Panel physicians must [request a consultation](#) from the Tuberculosis Centers of Excellence (COEs). If treatment is managed by a national program, the panel physician is required to follow the treatment course, consult COEs, and alert DGMQ if the treatment is not consistent with US requirements.

Additional written guidance on treatment of drug-resistant tuberculosis disease can be found in [Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, 3rd edition](#), by the Curry International Tuberculosis Center and California Department of Public Health.

Applicants who are on tuberculosis disease treatment at the time of the examination must be transferred into a DGMQ-defined [DOT](#) program provided by, or closely monitored by, the panel physician for the remainder of treatment, and have the following performed:

- Chest radiograph
- Three sputum specimens for AFB smear and mycobacterial culture
- DST on positive isolates

When applicants on tuberculosis disease treatment at the time of examination have negative smears and cultures at the time of diagnosis, and remain culture-negative, panel physicians should use their clinical judgment to determine whether continued tuberculosis disease treatment is warranted. If panel physicians feel that further treatment is not clinically warranted, these applicants must be given a Class B1 TB, Pulmonary classification.

The panel physicians must provide DGMQ-defined [DOT](#) at their clinics to applicants, or refer the applicant to a program that will provide DGMQ-defined [DOT](#) consistent with these Technical Instructions. When applicants are sent for treatment at national or other in-country programs for DOT, panel physicians must first ensure that the programs provide DGMQ-defined [DOT](#), and treatment regimens are consistent with ATS/CDC/IDSA standards. The panel physician must then collaborate with these designated treatment programs to ensure adequate completion of therapy for the applicants by reviewing treatment and testing records once a month at a minimum, and additional measures deemed appropriate.

It is the panel physician's responsibility to ensure that all applicants have an option to receive DGMQ-defined [DOT](#) treatment if they are diagnosed with tuberculosis disease. Panel physicians must work with their national programs and colleagues to identify DGMQ-defined [DOT](#) options in multiple regions of the country to accommodate applicants when possible. The panel physician must also explain to the applicants at the time of diagnosis that if they refuse to be treated at a site that provides DGMQ-defined [DOT](#) treatment consistent with the Technical Instructions for the full duration of therapy, the applicant will be required to wait 1 year after treatment completion before they can be allowed to repeat the medical screening. For example, an applicant prescribed a 6 month treatment course would need to wait 1 year and 6 months before medical screening could be completed. Applicants refusing DGMQ-defined [DOT](#) must sign a form stating that they refuse to be treated by DOT, and acknowledging that they are aware of the DOT treatment option, that documentation of treatment is required, and understand the required wait time.

All applicants who refuse DGMQ-defined [DOT](#) must provide detailed documentation of their treatment to demonstrate having completed tuberculosis disease treatment. A letter from a physician stating they were treated is not sufficient. Documentation of treatment must include:

- Medication names
- Medication dosages
- Dates of delivery of each medication
- All sputum smear, culture, and DST results performed by the treatment center
- Reports of all chest x-rays performed by the treatment center

The applicant's treatment location, including physician name and clinic city and state, must be documented on the DS Forms. The applicant must provide this detailed report to the panel physician for review and the report must be attached to the travel documents of the applicant. Without this documentation, the applicant will not be considered further for immigration to the United States. Please note that applicants who completed treatment for tuberculosis disease before their first immigration medical examination are not subject to this wait time.



## WAIVERS

A provision allows applicants undergoing tuberculosis disease treatment to petition for a Class A waiver.

In exceptional situations, a provision allows applicants undergoing tuberculosis disease treatment to petition for a Class A waiver. Forms must be completed by the applicants, Form I-601 for immigrants, and Form I-602 for refugees. The US Department of Homeland Security (DHS) reviews these petitions and considers them in situations with extenuating circumstances. DGMQ reviews each petition and provides an opinion regarding the case to the requesting entity (US Department of State or DHS). DHS then has the final authority to approve or deny the waiver request.

All requests for waivers need to be accompanied by written approvals from both the US-based physician accepting responsibility for the applicant's continued care and treatment and the US local and state health departments with jurisdiction.

As soon as the panel physician is aware that an applicant has applied for a Class A waiver, the panel physician must provide the following to CDC so that CDC can review the case and make a recommendation to DHS:

- Summary of case
- Completed DS forms
- All available pertinent laboratory results
- All chest x-ray images (in a DICOM format)

## TUBERCULOSIS TREATMENT MONITORING

The frequency of laboratory testing required during treatment is based on drug-susceptibility testing results.

Children <10 years of age with drug-susceptible or culture-negative tuberculosis disease who cannot provide sputum specimens will not need to provide induced sputum or gastric aspirate specimens during treatment, unless their clinical course warrants further evaluation.

When signs of clinical worsening or failure to improve occur during therapy, such as persistent weight loss, fever, cough, or worsening chest x-ray, repeat sputum smears, cultures, and DST are indicated.



These guidelines for treatment monitoring differ from recommendations in the [ATS/CDC/IDSA guidelines](#) and [Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, 3rd edition](#), by the Curry International Tuberculosis Center and California Department of Public Health.

- **Culture-positive and rifampin-sensitive:** two sputum specimens must be collected and submitted for AFB microscopy and mycobacteria culture once a month during therapy until cultures are negative for 2 consecutive months. Two sputum specimens must be collected and submitted for AFB microscopy and mycobacteria culture at the end of therapy. See the [sputum collection](#) section for additional information about sputum collection.
- **Culture-positive and rifampin-resistant:** two sputum specimens must be collected and submitted for AFB microscopy and mycobacteria culture once a month during therapy. Two sputum specimens must be collected and submitted for AFB microscopy and mycobacteria culture at the end of therapy.
- **No drug susceptibility testing results (culture-negative or contamination on DST specimen):** one sputum specimen must be collected and submitted for AFB microscopy and mycobacteria culture once a month during therapy. Two sputum specimens must be collected and submitted for AFB microscopy and mycobacteria culture at the end of therapy.

## CONTACTS OF TUBERCULOSIS CASES

Contacts of persons with tuberculosis disease should be removed from exposure to the person with tuberculosis disease if possible.

All contacts must receive an IGRA (or TST if IGRA unavailable) within 2 weeks of diagnosis of the potential source case.

Contacts who have clinical or chest x-ray findings suggestive of tuberculosis disease, or known HIV infection must provide at least three sputum specimens for AFB microscopy and mycobacteria culture.

A contact is a person who has shared the same enclosed air space in a household or other enclosed environment for a prolonged period (days or weeks, not minutes or hours) with a person with smear-positive or culture-positive tuberculosis disease. Contacts are at increased risk of infection with *M. tuberculosis*. The end of contact occurs when the person with tuberculosis disease is isolated from others or the person's sputum smears are negative after at least 2 weeks of treatment.

Applicants for US immigration who are contacts must be evaluated for tuberculosis disease by the panel physician. All such contacts must receive an IGRA (use TST for contacts only if IGRA is unavailable).

If the IGRA is negative (or TST <5 mm if IGRA not available), negative chest x-ray (if required), no signs or symptoms of TB, and no known HIV infection, the contact may be cleared for travel immediately. These applicants must be assigned a Class B3 TB, Contact Evaluation classification if traveling <8 weeks after contact ends. If the IGRA is negative, and the contact is not placed on prophylaxis and does not choose to travel immediately, the IGRA should be repeated every 3 months until departure (if exposure continues) or until ≥8 weeks after contact ends, or the IGRA becomes positive. Contacts who travel ≥8 weeks after contact ends and have an IGRA done ≥8 weeks after the end of contact that is negative, should not receive a Class B3 TB, Contact Evaluation classification.

If the IGRA is positive (or TST ≥5 mm if IGRA not available), the contact must be further evaluated with medical history, physical examination, and chest x-ray. Contacts with clinical findings or chest x-ray suggestive of tuberculosis disease, or known HIV infection must provide three sputum specimens to undergo microscopy for AFB and culture for *M. tuberculosis*. Contacts diagnosed with tuberculosis disease must receive a Class A TB classification and must complete tuberculosis disease treatment before US immigration.

If the IGRA is positive, but the chest x-ray is negative, there are no signs or symptoms of TB, and no known HIV infection, the applicant must receive a classification of B2, LTBI evaluation and B3, Contact Evaluation and can be immediately cleared to travel. If the applicant chooses not to travel immediately, and is not started on LTBI treatment, repeat evaluation including medical history, physical examination, and chest x-ray is recommended, but not required, every 3 months until departure. The classification for contacts with a positive IGRA result and no findings of tuberculosis disease will remain B2, LTBI evaluation and B3, Contact Evaluation.

Contacts who have either a positive or negative IGRA, who had clinical findings or chest x-ray suggestive of tuberculosis disease and had a negative sputum analysis for AFB and mycobacteria culture must be classified as both Class B1 TB, Pulmonary, and Class B3 TB, Contact Evaluation if traveling less than 8 weeks after contact has ended.

Situations in which preventive therapy should be initiated overseas include certain pediatric contacts (see information below) and contacts with impaired immunity (e.g., HIV infection).

- Children <4 years of age and applicants with impaired immunity (e.g., HIV infection) who are contacts of a known tuberculosis disease case, regardless of how that case was diagnosed, and who have a negative evaluation for tuberculosis disease, should begin directly observed preventive therapy (DOPT) regardless of IGRA results. Isoniazid may be used except in known exposures to a tuberculosis disease case with MDR TB or isoniazid resistance. Advice on other preventive regimens should be sought from experts at a [COE](#).
- Children and applicants with impaired immunity (e.g., HIV infection) receiving preventive therapy should have an IGRA 8 weeks after exposure to the infectious case ends. Preventive therapy may be discontinued if the IGRA is negative 8 weeks after exposure to the infectious case ends.
- Children and applicants with impaired immunity may be cleared for travel while on preventive therapy and should be assigned a tuberculosis classification (Class B3 TB, Contact Evaluation). If the applicant does not complete preventive therapy before departure, a 30-day supply of medication and instructions on how to take it should be given to the applicant or the parent or responsible adult traveling with the applicant.

Panel physicians do not need to wait to classify applicants who are a contact of someone suspected of having tuberculosis disease until the person they are a contact to has culture results returned. If someone leaves for the United States and you later learn that he or she is a contact of someone with a positive culture, please notify DGMQ ([cdcQAP@cdc.gov](mailto:cdcQAP@cdc.gov)), who will then notify the receiving health department.



## DOCUMENTATION

All medical documentation, including original laboratory reports, must be included with the required DS forms.

All required medical documentation must be sent by courier or other secure means to the US Embassy for all Class A and Class B1 conditions. All Class A and Class B1 tuberculosis conditions must be reported to the US Embassy upon detection.

Department of State forms DS-2054, DS-3025, DS-3026, and DS-3030, and DICOM images of chest radiographs, which applicants are required to carry to their US destination, must be completed in their entirety and included in the applicant's travel packet. This includes assigning a tuberculosis classification on the DS-2054 and DS-3030. Incomplete documentation may result in refusal to grant a visa or in designation of medical hold status at arrival to ports of entry.

For applicants requiring tuberculosis disease treatment before US immigration, the panel physician is required to document the following:

1. **Chest radiograph findings and images** before, during, and after treatment.
2. **Interferon gamma release assay** results must include type of IGRA used (i.e., QuantiFERON® or T-SPOT®), expiration date, and test result including units of measurement. If no IGRA is licensed for use in the country of exam, TST documentation must include date of TST reading, name of product, expiration date, the type of product used (e.g., 5TU PPD-S), and results in millimeters of induration.
3. **Sputum smear** AFB microscopy results obtained before, during, and after treatment
4. **Cultures for mycobacteria** results obtained before, during, and after treatment, including cultures that were contaminated
5. **Drug susceptibility test results** performed on any positive cultures
6. **DOT regimen** received (including doses of all medications), start date, and completion date, and any periods of interruption. Daily DOT record must also be included.
7. **Clinical course**, such as clinical improvement or lack of improvement during and after treatment, including resolution of symptoms and signs and weight stability or gain

## TUBERCULOSIS INDICATORS

DGMQ is responsible for monitoring the effectiveness of these Technical Instructions in diagnosing applicants with tuberculosis. To assist with this monitoring, panel physicians must submit Tuberculosis Indicator reports to CDC/DGMQ annually. The reporting form and instructions are e-mailed to panel physicians at the end of each calendar year. Reports are due in March. Panel physicians who do not receive the reporting form by January of each year, or are new to the data submission process, should contact [cdcQAP@cdc.gov](mailto:cdcQAP@cdc.gov) for assistance.

## GLOSSARY OF ABBREVIATIONS

<b>ATS</b>	American Thoracic Society
<b>BCG</b>	Bacille Calmette-Guérin
<b>CDC</b>	US Centers for Disease Control and Prevention
<b>Chest x-ray</b>	Chest radiograph
<b>COE</b>	Tuberculosis Centers of Excellence
<b>DGMQ</b>	Division of Global Migration and Quarantine (CDC)
<b>DOPT</b>	Directly observed preventive therapy
<b>DOT</b>	Directly observed therapy
<b>DST</b>	Drug-susceptibility testing
<b>FDA</b>	US Food and Drug Administration
<b>GDF</b>	WHO Global Drug Facility
<b>HIV</b>	Human immunodeficiency virus
<b>IDA</b>	International Dispensary Association
<b>IDSA</b>	Infectious Diseases Society of America
<b>IGRA</b>	Interferon gamma release assay
<b>LTBI</b>	Latent tuberculosis infection
<b>MDR TB</b>	Multidrug-resistant tuberculosis disease
<b>PPD</b>	Purified protein derivative
<b>TST</b>	Tuberculin skin test
<b>WHO</b>	World Health Organization

## DEFINITIONS OF SELECTED TERMS

**Contact** – a person who has shared the same enclosed air space (i.e., exposed) in a household or other enclosed environment for a prolonged period (days or weeks, not minutes or hours) with a person with smear- or culture-positive pulmonary tuberculosis disease. Contacts exposed in this fashion to persons with smear- or culture-positive pulmonary tuberculosis disease are at increased risk of infection with *M. tuberculosis*.

**Directly observed therapy (DOT)** – adherence-enhancing strategy in which a health-care worker watches a patient swallow each dose of medication in person and documents the dose. Health-care workers providing DOT can include pharmacists, trained community health workers, etc., but can't include the applicant's friends or relatives. Directly observed therapy is the standard of care for all applicants with tuberculosis disease. Panel physicians must provide DOT treatment to applicants or identify in-country treatment programs that follow this definition of DOT. Treatment provided outside the panel physician clinic must be evaluated in advance and closely supervised by the panel physician to ensure compliance with this definition.

**Drug susceptibility test (DST)** – a laboratory determination to assess whether an *M. tuberculosis* complex isolate is susceptible or resistant to antituberculosis drugs. The results predict whether a specific drug is likely to be effective in treating tuberculosis disease caused by that isolate.

**Extensively drug-resistant tuberculosis disease (XDR TB)** – tuberculosis disease caused by *M. tuberculosis* organisms that are resistant to isoniazid and rifampin, plus resistant to any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin).

**Extrapulmonary tuberculosis** – tuberculosis disease in any part of the body other than the lung parenchyma, pleura, intrathoracic lymph nodes or larynx. The presence of extrapulmonary disease does not exclude pulmonary tuberculosis disease.

**Interferon gamma release assay (IGRA)** – test that measure a component of cell-mediated immunity reactivity to *M. tuberculosis* in fresh whole blood.

**Latent tuberculosis infection (LTBI)** – Latent tuberculosis infection (LTBI) is the presence of *M. tuberculosis* in the body without signs and symptoms, or radiographic or bacteriologic evidence of tuberculosis disease or extrapulmonary tuberculosis.

**Multidrug-resistant TB (MDR TB)** – tuberculosis disease caused by *M. tuberculosis* organisms that are resistant to at least isoniazid and rifampin.

***M. tuberculosis* culture** – a laboratory test in which the organism is grown from a submitted specimen (e.g., sputum) to determine the presence of *M. tuberculosis*. In the absence of cross contamination, a positive culture confirms the diagnosis of tuberculosis disease.

**Pre-immigration medical screening** – the medical evaluation required for all applicants.

**Successfully completed tuberculosis disease therapy** – Directly observed therapy for tuberculosis disease taken for the full duration of therapy, including the total number of recommended doses within the time specified in [ATS/CDC/IDSA guidelines](#), with negative sputum smears and cultures at completion.

**Tuberculosis disease** – disease caused by infection with a member of the *M. tuberculosis* complex that has progressed to causing clinical (manifesting symptoms or signs) or subclinical (early stage in which signs or symptoms are not present, but other indications of disease activity are present) illness. For the purpose of this document, tuberculosis disease refers to disease of the lung parenchyma, pleura, intrathoracic lymph nodes and larynx. Latent tuberculosis infection and extrapulmonary tuberculosis are not included in this definition of tuberculosis disease.







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