# CDC IMMIGRATION REQUIREMENTS:

# Technical Instructions for Tuberculosis Screening and Treatment

## 2007

# Table of Contents



# Figures



# Tables

# Preface

The medical screening for tuberculosis among persons overseas applying for U.S. immigration status and non-immigrants who are required to have an overseas medical examination, heretofore 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 detect and treat tuberculosis disease among applicants and to reduce the risk of spread of tuberculosis among the U.S. population after immigration.

The instructions in this document supersede all previous 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 screening and treatment among all applicants.

For any questions about these Technical Instructions, please contact the Immigrant, Refugee, and Migrant Health Branch of the Division of Global Migration and Quarantine, Centers for Disease Control and Prevention, at 404-498-1600.

# Tuberculosis Screening

**Any applicant for whom the clinical suspicion of tuberculosis is high enough to warrant treatment for tuberculosis disease, regardless of laboratory results, is considered to have a diagnosis of tuberculosis.**

**Applicants 2-14 years of age living in countries with a World Health Organization (WHO)-estimated tuberculosis incidence rate of ≥20 cases per 100,000 population should have a tuberculin skin test.**

**Prior receipt of Bacille Calmette-Guérin (BCG) vaccination does not change the screening requirements or the required actions based on tuberculin skin test results.**

A complete screening medical examination for tuberculosis consists of a medical history, physical examination, chest radiography ([CXR], when required), determination of immune response to *Mycobacterium tuberculosis* antigens (i.e., tuberculin skin testing [TST], when required), and laboratory testing for human immunodeficiency virus (HIV) infection (for applicants ≥15 years of age) and *M. tuberculosis* (when required, Figures 1 and 2).

All applicants <15 years of age require a physical examination and history from a parent or responsible adult who knows the child best. Applicants <15 years of age who are ill and have signs or symptoms suggestive of tuberculosis should have a TST. If the TST is ≥5 mm, a CXR (anteroposterior or posteroanterior view and a lateral view for applicants <10 years of age; posteroanterior view for applicants ≥10 years of age) should be performed. An exam shall include three sputum specimens to undergo microscopy for acid-fast bacilli (AFB), as well as culture for mycobacteria and confirmation of the *Mycobacterium* species, at least to the *M. tuberculosis* complex level, and any laboratory or additional studies that are deemed necessary, either as a result of the physical examination or pertinent information elicited from the applicant's medical history for the panel physician to reach a conclusion about the presence or absence of tuberculosis, but see 42 CFR 34.3(b)(v).

Applicants <15 years of age who are a known contact of someone with recently diagnosed tuberculosis should have a TST. If the TST is ≥5 mm, a CXR (anteroposterior or posteroanterior view and a lateral view for applicants <10 years of age; posteroanterior view for applicants ≥10 years of age) should be performed. If the CXR findings are suggestive of tuberculosis, the applicant should provide three sputum specimens to undergo microscopy for AFB, as well as culture for mycobacteria and confirmation of the *Mycobacterium* species, at least to the *M. tuberculosis* complex level.

Applicants ≥15 years of age require a medical history, physical examination, and CXR. If the applicant has a CXR with findings suggestive of tuberculosis, has signs and symptoms of tuberculosis, or has HIV, the applicant should provide three sputum specimens to undergo microscopy for AFB, as well as culture for mycobacteria and confirmation of the *Mycobacterium* species, at least to the *M. tuberculosis* complex level.

Applicants 2-14 years of age living in countries with a World Health Organization (WHO)-estimated tuberculosis incidence rate of ≥20 cases per 100,000 population should have a TST. If the TST is ≥5 mm, a CXR (anteroposterior or posteroanterior view and a lateral view for applicants <10 years of age; posteroanterior view for applicants ≥10 years of age) should be performed. If the CXR findings are suggestive of tuberculosis, the applicant should provide three sputum specimens to undergo microscopy for AFB, as well as culture for mycobacteria and confirmation of the *Mycobacterium* species, at least to the *M. tuberculosis* complex level.

Pulmonary tuberculosis is a disease that involves the lung parenchyma and is often infectious (i.e., contagious [determined by sputum smear examination for AFB and mycobacterial culture]). Laryngeal tuberculosis is rare but highly infectious. Because the emphasis for pre-immigration medical evaluation is on infectiousness, for the purpose of this document pulmonary tuberculosis refers to both disease of the lung parenchyma and laryngeal tuberculosis. Furthermore, panel physicians should be aware that disease of the lung parenchyma may occur concurrently with pleural tuberculosis, and the parenchymal lung disease may not be apparent on chest radiograph due to compression of affected lung tissue by pleural fluid.

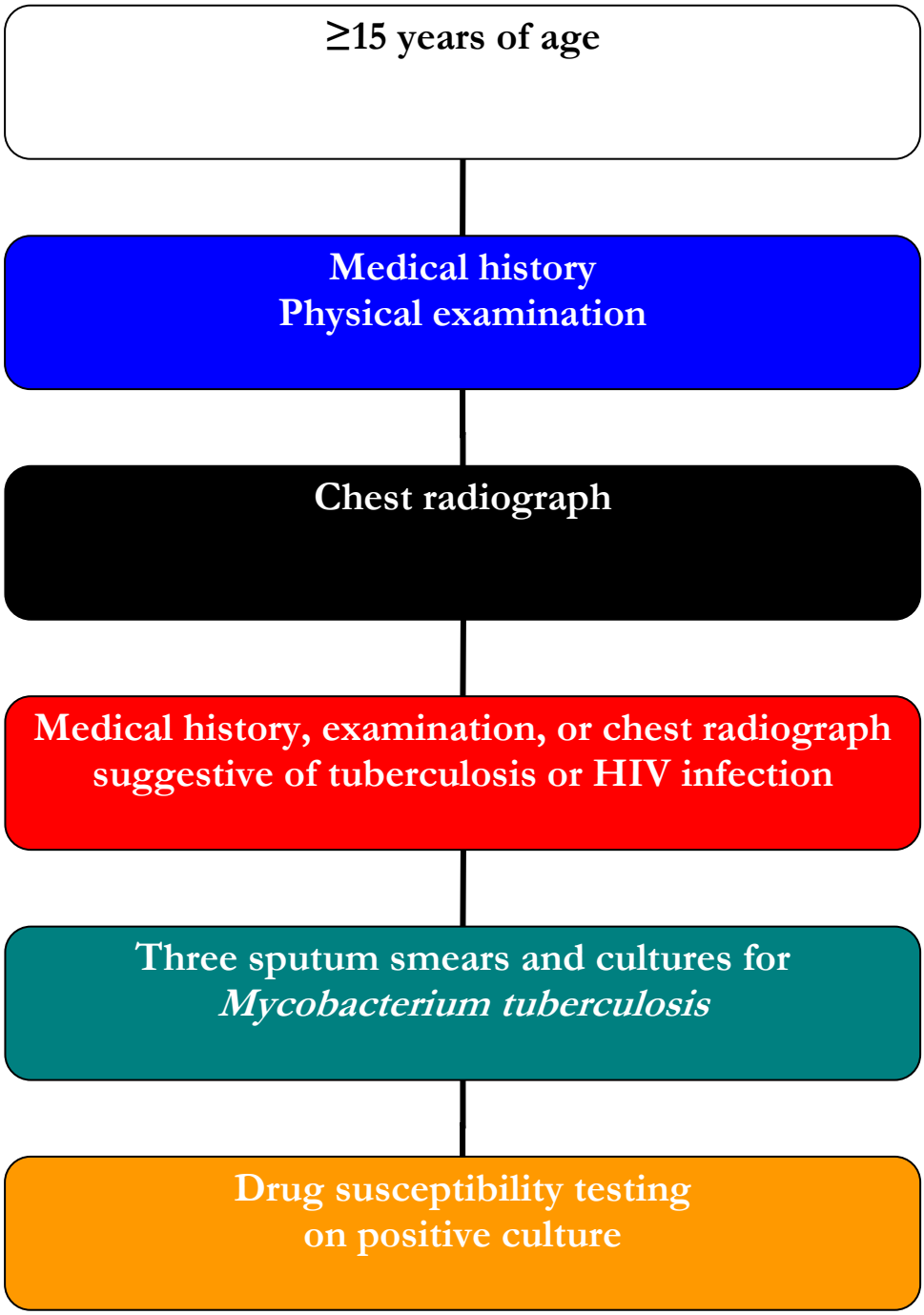


**Figure 1: Tuberculosis screening medical examination for applicants in countries with a WHO-estimated tuberculosis incidence rate <20 cases per 100,000 population.**

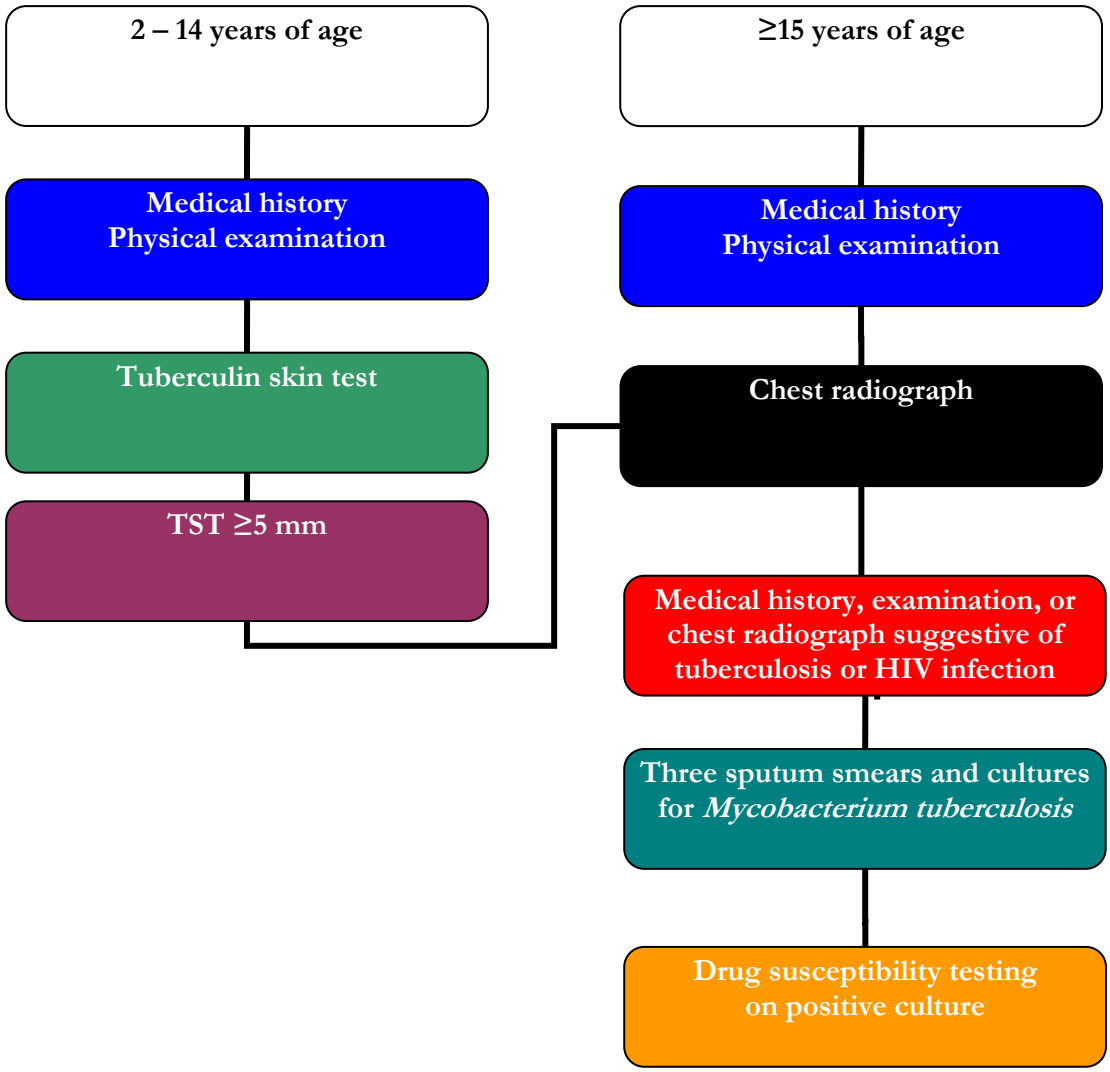


**Figure 2: Tuberculosis screening medical examination for applicants in countries with a WHO-estimated tuberculosis incidence rate ≥20 cases per 100,000 population.**

Each aspect of the examination is detailed below:

## Medical History

- The medical history should focus on risk factors for tuberculosis disease, including previous history of tuberculosis; illness suggestive of tuberculosis (such as cough of >3 weeks duration, dyspnea, weight loss, fever, or hemoptysis); prior treatment suggestive of tuberculosis treatment; and prior diagnostic evaluation suggestive of tuberculosis. The clinical expression of tuberculosis may be different in children than 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 or illness, treatment, or diagnostic evaluation suggestive of tuberculosis.
- Prior receipt of Bacille Calmette-Guérin (BCG) vaccination should be ascertained; review and record if documentation and date of receipt are available.

## Physical Exam

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

## Chest Radiography

When performed, chest radiography (CXR) should consist of a standard posteroanterior view for all applicants 10 years of age and older. Applicants <10 years of age who receive a CXR should have a standard anteroposterior or standard posteroanterior view; they should also have a lateral view. If a child receives a posteroanterior view, the CXR should be labeled "PA" for the benefit of radiologist's review.

Chest radiographs should be interpreted by a radiologist and reviewed by the panel physician. Documentation of the results for the chest radiographs should be available within 1 week from the time the CXR was performed. Chest radiographs of any applicants, especially children, should be re-taken if the initial CXR is suboptimal due to factors such as incorrect penetration or motion artifact. Chest radiograph interpretations should include comparisons with prior chest radiographs, if available.

Women who are pregnant are required to have a CXR to immigrate. Pregnant women will need to provide consent for the CXR. Pregnant women receiving chest radiographs should be provided abdominal and pelvic protection with double layer, wrap-around lead shields.

## Immune Response to *M. tuberculosis* Antigens

- Determination of immune response to *M. tuberculosis* antigens should be performed by placing a TST. Purified protein derivative (PPD [equivalent to 5TU PPD-S]) should be administered intradermally by the Mantoux method. Exceptions include applicants with written documentation from a physician of previous tuberculosis or for whom the measurement of the millimeters of induration is documented.
- The QuantiFERON®-TB Gold (QFT-G) test is a new blood test that has been approved by the U.S. Food and Drug Administration as an aid for detecting latent *M. tuberculosis* infection (LTBI). The assay measures a component of cell-mediated immune reactivity to *M. tuberculosis* in fresh whole blood. However, the role of QFT-G in overseas screening has not yet been defined, and the test requires laboratory capability that is not widely available. When a form of the test becomes available that requires less sophisticated laboratory capabilities, the QFT-G test, rather than the TST, may become the preferred test or an alternative to help diagnose LTBI. If such a change occurs, an update will be made to these Technical Instructions. Until such change is made, the TST is the required method.

## Laboratory Testing

- In addition to laboratory testing for HIV infection (see Technical Instructions for Human Immunodeficiency Virus Infection), when applicable, laboratory examination for tuberculosis disease should consist of at least three sputum specimens, which undergo microscopy for AFB as well as culture for mycobacteria and confirmation of the *Mycobacterium* species, at least to the *M. tuberculosis* complex level (Appendix B, Appendix C). Panel physicians must receive finalized culture results within 8 weeks of collection.
- 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 [Appendix C]) in order to determine their tuberculosis status and clear them for travel.
- Positive *M. tuberculosis* cultures shall undergo drug susceptibility testing (DST) for isoniazid, rifampin, ethambutol, pyrazinamide, and streptomycin. Panel physicians must have access to DST results within 3 months of sputum collection.
- Positive *M. tuberculosis* cultures that are resistant to isoniazid and rifampin shall undergo drug susceptibility testing on second-line tuberculosis medications.

In addition to the recommendations provided, panel physicians should use their clinical judgment in the evaluation and treatment of the applicant.

Many applicants may have previously received Bacille Calmette-Guérin (BCG) vaccination. Prior receipt of BCG does not change the screening requirements or the required actions based on those results.

Detection of tuberculosis disease necessitates a combined clinical and public health response to cure individual tuberculosis patients, stop transmission, and enable safe movement to the United States.

Additional guidance for resettlement of large refugee groups is located in Appendix E.

## Pre-Departure Evaluation

**Additional screening immediately prior to departure (pre-departure evaluation) may be required in the event of an outbreak of tuberculosis disease or in the setting of extremely elevated rates of tuberculosis disease.**

**When applied, pre-departure evaluations serve as an additional measure to prevent importation of tuberculosis disease into the United States.**

**If the need arises, CDC will inform the Department of State to implement pre-departure evaluations.**

When pre-departure evaluations are required, they shall be performed on applicants who are Class B1 TB, Pulmonary. The evaluations shall be performed within 3 weeks of departure. The pre-departure evaluation shall consist of a medical history, physical examination, CXR, three sputum specimens for AFB microscopy (but no cultures required).

## Tuberculosis Screening Results and Travel Clearance

**The evaluation is complete when all required aspects of the medical examination have been completed, including final report of culture results, and the applicant can be assigned a Tuberculosis Classification.**

**Travel clearances are valid for 6 months from the time the evaluation is complete for applicants who have no Tuberculosis Classification or only Class B2 TB or Class B3 TB and who do not have HIV infection.**

**Travel clearances are valid for 3 months from the time the evaluation is complete for applicants who are Class B1 TB, Pulmonary or Class B1 TB, Extrapulmonary or who have HIV infection.**

**Applicants not traveling within the clearance period will need to restart the tuberculosis screening process.**

**Any applicant diagnosed with pulmonary or laryngeal tuberculosis who needs treatment is not cleared for travel until completion of successful treatment, regardless of the diagnostic criteria.**

It is important that tuberculosis disease be correctly diagnosed among applicants for U.S. immigration. Correct diagnosis of tuberculosis will ensure that applicants with tuberculosis disease receive correct treatment, reduce further spread of the disease, and reduce the likelihood of treating applicants who do not have the disease, thus unnecessarily delaying their immigration.

Applicants with clinical and radiographic findings suggestive of common bacterial infections of the upper and lower 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 tuberculosis therapy and their use could result in mistreatment of tuberculosis and lead to drug-resistant tuberculosis. After treatment for lower respiratory infections, the CXR for medical screening should not be performed until at least 8 weeks after therapy, unless the applicant's clinical status warrants further evaluation earlier than 8 weeks after therapy. Table 1 lists screening results and required actions for those results.

| Medical History | Physical Exam | Chest Radiograph | HIV Infection | Sputum Smears | Culture for Mycobacterium | Travel Clearance | Action or TB Classification |
|---|---|---|---|---|---|---|---|
| Normal | Normal | Normal | No | NA | NA | 6 months† | No TB Classification |
| Normal | Normal | Normal | Yes | Negative | Negative | 3 months† | No TB Classification‡ |
| Normal | Normal | Normal | Yes | Either positive | | No | Class A, Treatment |
| Any component suggestive of TB | | | No | Negative | Negative | No | Use clinical judgment§ |
| Any component suggestive of TB | | | No | Either positive | | No | Class A, Treatment |
| Any component suggestive of TB | | | Yes | Negative | Negative | No | Use clinical judgment‡,§ |
| Any component suggestive of TB | | | Yes | Either positive | | No | Class A, Treatment |
| Completed therapy for tuberculosis | | | | Negative | Negative | 3 months¶ | Class B1 TB, Pulmonary |
| Completed therapy for tuberculosis | | | | Either positive | | No | Class A, Treatment |

**Table 1: Tuberculosis screening results,* travel clearance, and actions.**

* When required, TST results have no bearing on travel clearance.

† From the time the evaluation is complete. When needed, culture results must be known within 8 weeks of collection.

‡ Applicant has a Class A HIV classification.

§ Applicants with equivocal results may have additional diagnostic tests (e.g., repeat sputum smears, cultures and CXR) performed to diagnose tuberculosis disease. Tuberculosis treatment should not be initiated on applicants who are smear- and culture-negative unless the CXR and clinical findings are highly suggestive of tuberculosis disease. If cleared to travel, their tuberculosis classification will be Class B1 TB, Pulmonary.

¶ Travel clearance is for 3 months from the time the evaluation is complete; culture results must be known within 8 weeks of collection.

## Screening Results and Travel Clearance

- Applicants without clinical findings of tuberculosis, without HIV infection, and with a normal CXR (and a TST <10 mm in children 2-14 years of age [when applicable]) can be cleared for travel to the United States (Table 1). Applicants should be assigned a tuberculosis classification (No TB Classification, Appendix F).

- When applicable, applicants 2-14 years of age who have a TST ≥10 mm and are without HIV infection (if tested), have no clinical findings of tuberculosis, and have a normal CXR can be cleared for travel to the United States. Such applicants should be assigned a tuberculosis classification to receive evaluation for LTBI in the United States (Class B2 TB, LTBI Evaluation).

- Applicants <15 years of age who are ill and have signs or symptoms suggestive of tuberculosis should have a TST. If the TST is ≥5 mm, a CXR (anteroposterior or posteroanterior view and a lateral view for applicants <10 years of age; posteroanterior view for applicants ≥10 years of age) should be performed. An exam shall include three sputum specimens to undergo microscopy for acid-fast bacilli (AFB), as well as culture for mycobacteria and confirmation of the *Mycobacterium* species, at least to the *M. tuberculosis* complex level, and any laboratory or additional studies that are deemed necessary, either as a result of the physical examination or pertinent information elicited from the applicant's medical history for the panel physician to reach a conclusion about the presence or absence of tuberculosis, but see 42 CFR 34.3(b)(v) (TB classification pending).

- Applicants with HIV infection (see Technical Instructions for Human Immunodeficiency Virus Infection) should have three sputum specimens sent to the laboratory for AFB microscopy and culture. These applicants cannot be cleared for travel until the results of the laboratory investigation are available (TB classification pending).

- Applicants who have sputum smears that are positive for AFB microscopy should not be cleared for travel and should be treated for tuberculosis, unless non-tuberculous mycobacterial disease is diagnosed by culture or molecular methods (Class A TB).

- Applicants who have negative sputum smears and positive *Mycobacterium* cultures should not be cleared for travel and should be treated for tuberculosis (Class A TB).

- Applicants with equivocal results (e.g., who have findings suggestive of tuberculosis on medical history, physical exam, or CXR, but who do not have positive sputum smears or positive cultures) may have additional diagnostic tests (such as repeat sputum smears, cultures, or chest radiographs) performed to diagnose tuberculosis disease (if evaluation negative, Class B1 TB, Pulmonary).

- Applicants diagnosed with extrapulmonary tuberculosis only (except for laryngeal tuberculosis) can be cleared for travel. Applicants should be assigned a tuberculosis classification (Class B1 TB, Extrapulmonary). Efforts should be made to obtain a laboratory confirmed diagnosis. Applicants with extrapulmonary tuberculosis should be considered for treatment if departure is not planned within 3 months or if withholding therapy would be harmful. Applicants with extrapulmonary disease who are started on therapy prior to departure must complete therapy after their arrival in the United States. They should be given a 30-day supply of medication at departure. Because patients with laryngeal tuberculosis can transmit tuberculosis to others, applicants with laryngeal tuberculosis should complete therapy before departure.

- A diagnosis of extrapulmonary tuberculosis does not preclude an evaluation for pulmonary tuberculosis within the specified time frames. Applicants with extrapulmonary tuberculosis (except for laryngeal tuberculosis) do not have to provide sputum smears unless they have an abnormal CXR suggestive of tuberculosis or have HIV.

# Tuberculosis Treatment

**All applicants with pulmonary or laryngeal tuberculosis disease who need treatment overseas will need to complete directly observed therapy (DOT) prior to U.S. immigration.**

**Applicants diagnosed with tuberculosis disease who are smear and culture negative should not have treatment begun overseas unless the CXR and clinical findings are highly suggestive of tuberculosis disease.**

**Follow current ATS/CDC/IDSA guidelines (http://www.cdc.gov/nchstp/tb/pubs/mmwrhtml/Maj_guide/Treatment.htm).**

**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.**

**For panel physicians not wanting to treat tuberculosis patients themselves, the Division of Global Migration and Quarantine will identify national or other in-country programs that follow these standards. Treatment will need to be supervised by panel physicians using these standards or by programs identified by the Division of Global Migration and Quarantine.**

Treatment of tuberculosis, both pulmonary and extrapulmonary, should be administered following DOT policies and practices during the entire courses of therapy. DOT is an adherence-enhancing strategy in which a health-care worker or other trained person watches a patient swallow each dose of medication. Directly observed therapy is the standard care for all applicants with tuberculosis disease.

Applicants with positive sputum smears or positive cultures who do not want to be treated may not travel to the United States. Moreover, applicants with a history of noncompliance may not be cleared for travel until they have completed directly observed therapy (DOT). The panel physician has an ethical obligation to make all efforts to treat patients, including notifying public health officials if all efforts to treat them fail. Panel physicians should notify the appropriate public health officials in their jurisdiction when they diagnose an applicant with tuberculosis disease.

Applicants, including children, who are diagnosed with tuberculosis disease but have negative sputum smears and negative cultures should receive consideration for not initiating therapy prior to departure. Treatment should only be initiated if the CXR and clinical findings are highly suggestive of tuberculosis disease. Applicants who are begun on therapy following three negative sputum smears and after subsequent sputum culture results are found to be negative should be re-evaluated clinically, radiographically, and with TST. Treatment should be continued only if there is evidence of clinical and/or radiographic improvement.

Treatment of U.S. applicants should be administered consistent with the current American Thoracic Society/CDC/Infectious Diseases Society of America guidelines for treatment of tuberculosis, including being guided by drug-susceptibility testing results (http://www.cdc.gov/nchstp/tb/pubs/mmwrhtml/Maj_guide/Treatment.htm). These guidelines are consistent with International Standards for Tuberculosis Care (Tuberculosis Coalition for Technical Assistance, The Hague: 2006).

Treatment of drug-resistant and multidrug-resistant tuberculosis (MDR TB) should be done by or in close consultation with experts in the management of such cases and in coordination with the Division of Global Migration and Quarantine (DGMQ). Panel physicians and DGMQ-identified treatment programs should have direct access to tuberculosis treatment expertise for consultation regarding care of complex tuberculosis cases. DGMQ, in consultation with the Division of Tuberculosis Elimination (DTBE), will identify tuberculosis consultants. Documentation of consultation with a tuberculosis expert should be maintained and forwarded by the panel physician to DGMQ within 1 week of consultation. Additional written guidance on treatment of drug-resistant tuberculosis can be found in "Drug-resistant tuberculosis: a survival guide for clinicians" by the Francis J. Curry National Tuberculosis Center and California Department of Health Services, San Francisco, California (www.nationaltbcenter.edu).

For panel physicians who do not want to perform tuberculosis therapy, DGMQ will identify programs which adhere to these standards. When applicants are sent for treatment to national or other in-country programs, panel physicians will need to understand that their role is that of a referring physician and they still have responsibility for the adequate completion of therapy for the applicants. Panel physicians will need to ensure that anti-fraud measures are in place for their patients.

## Waivers

**A provision allows applicants undergoing pulmonary or laryngeal tuberculosis treatment to petition for a Class A waiver.**

**Waivers should be pursued for any immigrant or refugee who has a complicated clinical course and would benefit from receiving treatment of their tuberculosis in the United States.**

**Applicants diagnosed with tuberculosis disease who are both smear- and culture-negative and will be traveling to the United States prior to start of treatment do not need to complete the waiver process.**

In exceptional medical situations, a provision allows applicants undergoing pulmonary tuberculosis treatment to petition for a Class A waiver. These petitions are reviewed by the Department of Homeland Security on an individual basis and considered in situations with extenuating medical circumstances. Form I-601 or I-602 (for immigrants or refugees, respectively) must be completed.

All requests for waivers need to be accompanied by prior notification and approval by the U.S.-based physician accepting responsibility for the applicant's continued care and treatment and the appropriate U.S. health department with jurisdiction.

Regardless of their tuberculosis classification, applicants who have HIV infection will have to obtain a Class A waiver for their HIV condition (refer to HIV Technical Instructions).

# Tuberculosis Treatment Monitoring

**These guidelines in the Technical Instructions use drug-susceptibility testing results to determine the frequency of laboratory testing during drug treatment.**

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

**When signs of clinical worsening occur during therapy, such as persistent weight loss, fever, cough, or worsening CXR, 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" by the Francis J. Curry National Tuberculosis Center and California Department of Health Services.

- **Drug-susceptible:** two sputum specimens should 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 should be collected and submitted for AFB microscopy and mycobacteria culture at the end of therapy.
- **Resistant to only one drug (including resistant to only isoniazid or rifampin):** two sputum specimens should 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 should be collected and submitted for AFB microscopy and mycobacteria culture at the end of therapy.
- **Resistant to more than one drug but susceptible to isoniazid or rifampin (drug resistant but not MDR TB):** two sputum specimens should 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 should be collected and submitted for AFB microscopy and mycobacteria culture at the end of therapy.
- **MDR TB (resistant at least to both isoniazid and rifampin):** two sputum specimens should be collected and submitted for AFB microscopy and mycobacteria culture once a month during therapy. Two sputum specimens should be collected and submitted for AFB microscopy and mycobacteria culture at the end of therapy.
- **No drug susceptibility testing results (culture negative):** one sputum specimen should be collected and submitted for AFB microscopy and mycobacteria culture once a month during therapy. Two sputum specimens should be collected and submitted for AFB microscopy and mycobacteria culture at the end of therapy.

## Contacts of Tuberculosis Cases

**Contacts of persons with pulmonary tuberculosis disease should be removed from exposure to the person with tuberculosis.**

**All contacts should receive a TST.**

**Contacts who have clinical findings or CXR findings suggestive of tuberculosis should 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 (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 a smear- and/or culture-positive pulmonary tuberculosis case. Contacts exposed in this fashion to persons with smear or culture positive pulmonary tuberculosis are at increased risk of infection with *M. tuberculosis*. The end of contact occurs when the tuberculosis case is isolated from others or the sputum cultures become negative.

Panel physicians should notify the appropriate public health authorities in their jurisdiction when they diagnose an applicant with pulmonary tuberculosis. Contacts of cases who are applicants for U.S. immigration should be evaluated for tuberculosis disease by the panel physician. All such contacts should receive a TST.

If the TST is ≥5 mm, the contact should be further evaluated with medical history, physical examination, and CXR. If the contact is not started on LTBI therapy, he or she should receive an evaluation with medical history, physical examination, and CXR every 3 months until departure.

If the TST is <5 mm and the contact is not placed on prophylaxis, the TST should be repeated every 3 months until ≥8 weeks after end of contact ends, the index case has negative sputum cultures for 2 consecutive months, or TST becomes ≥5 mm.

Contacts with clinical findings or CXR suggestive of tuberculosis disease should provide three sputum specimens to undergo microscopy for AFB and culture for mycobacterium. Contacts diagnosed with tuberculosis disease will need to complete tuberculosis treatment prior to U.S. immigration.

Contacts who have a negative evaluation for tuberculosis disease may be cleared for travel. These

applicants should be assigned a tuberculosis classification (Appendix F).

All contacts who travel <8 weeks after end of contact should receive a Class B3 TB, Contact Evaluation classification, and their TST results should be documented.

Contacts who travel ≥8 weeks after end of contact and have a TST done ≥8 weeks after the end of contact that is <5 mm should not receive a Class B3 TB, Contact Evaluation classification. If the TST is ≥5 mm, they should receive a Class B3 TB, Contact Evaluation classification.

Contacts who had clinical findings or CXR suggestive of tuberculosis and had a negative sputum analysis for AFB and mycobacteria culture should be classified as Class B1 TB, Pulmonary, as specified earlier in these Technical Instructions.

In general, preventive therapy (i.e., treatment of LTBI) should not be initiated overseas. Exceptional situations in which preventive therapy should be initiated overseas include certain pediatric contacts (see next paragraph) 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 pulmonary tuberculosis case, regardless of how that case was diagnosed, and who have a negative evaluation for tuberculosis disease, should begin directly observed preventive therapy (DOPT) with isoniazid regardless of TST results. Because isoniazid is the medication for DOPT, isoniazid should not be administered if the known tuberculosis case has MDR TB or isoniazid resistance. Children and applicants with impaired immunity (e.g., HIV infection) receiving preventive therapy should have a TST 8 weeks after conclusion of exposure to the infectious case. Preventive therapy should be discontinued if the TST is <5 mm 8 weeks after conclusion of exposure to the infectious case. However, these children and applicants may be cleared for travel while on isoniazid and should be assigned a tuberculosis classification (Class B3 TB, Contact Evaluation) to ensure follow-up in the United States.

If an applicant does not complete preventive tuberculosis treatment prior to 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. All pertinent documentation should indicate the applicant's status so that the applicant can receive expedited follow-up upon arrival to the United States.

# Tuberculosis Classifications and Descriptions

**Applicants should be assigned one or more tuberculosis classifications. The applicant's classification should be recorded on the Tuberculosis Classification Cover Sheet (Appendix F)**

The tuberculosis classifications and descriptions are listed below:

### No TB Classification

Applicants with normal tuberculosis screening examinations.

### Class A TB with waiver

All applicants who have tuberculosis disease and have been granted a waiver.

### Class B1 TB, Pulmonary

No treatment

- Applicants who have medical history, physical exam, HIV, or CXR findings suggestive of pulmonary tuberculosis but have negative AFB sputum smears and cultures and are not diagnosed with tuberculosis or can wait to have tuberculosis treatment started after immigration.

Completed treatment

- Applicants who were diagnosed with pulmonary tuberculosis and successfully completed directly observed therapy prior to immigration. The cover sheet should indicate if the initial sputum smears and cultures were positive and if drug susceptibility testing results are available.

### Class B1 TB, Extrapulmonary

Applicants with evidence of extrapulmonary tuberculosis. Document the anatomic site of infection.

### Class B2 TB, LTBI Evaluation

Applicants who have a tuberculin skin test ≥10 mm but otherwise have a negative evaluation for tuberculosis. The size of the TST reaction, the applicant's status with respect to LTBI treatment, and the medication(s) used should be documented. For applicants who had more than one TST, whether the applicant converted the TST should be documented (i.e., initial TST <10 mm but subsequent TST ≥10 mm).

### Class B3 TB, Contact Evaluation

Applicants who are a recent contact of a known tuberculosis case. The size of the applicant's TST reaction should be documented. Information about the source case, name, alien number, relationship to contact, and type of tuberculosis should also be documented.

## Documentation

**All medical documentation, including original laboratory and chest radiograph reports, must be included with the required DS Forms.**

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

**All data that can be submitted electronically to CDC/DGMQ should be sent at the time of departure.**

Department of State forms DS-2053, DS-3024, DS-3025, and DS-3026 must be completed in their entirety and included in the applicant's travel packet. In addition, the panel physician is required to assign a tuberculosis classification for each applicant and complete the Tuberculosis Classification Cover Sheet, which should also be included in the applicant's travel packet. Incomplete documentation may result in refusal to grant visa or designation of medical hold status at arrival to ports of entry.

For applicants requiring tuberculosis treatment prior to U.S. immigration, the panel physician is required to document the following:

1. **Chest radiograph findings** before, during, and after treatment.
2. **Tuberculin skin test** documentation should include date of TST reading, name of product, expiration date, amount administered, and the type of product used (e.g., 5TU PPD-S), and results in millimeters.
3. **Sputum smear** AFB microscopy results obtained before, during, and after treatment.
4. **Cultures for mycobacteria** results obtained before, during, and after treatment, including those 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.
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.
8. **Pre-immigration medical screening** evaluations.
9. **Pre-departure screening** evaluations, when required by CDC (screening that is performed within 3 weeks of departure).

# APPENDIX A GLOSSARY OF ABBREVIATIONS

| | |
|---|---|
| ATS | American Thoracic Society |
| BCG | Bacille Calmette-Guérin |
| CDC | Centers for Disease Control and Prevention, United States |
| CXR | Chest radiograph |
| DGMQ | Division of Global Migration and Quarantine |
| DOPT | Directly observed preventive therapy |
| DOT | Directly observed therapy |
| DST | Drug-susceptibility testing |
| DTBE | Division of Tuberculosis Elimination |
| FDA | U.S. Food and Drug Administration |
| GAP | Global AIDS Program |
| GDF | WHO Global Drug Facility |
| HEPA | High-efficiency particulate air (filter) |
| HIV | Human immunodeficiency virus |
| IDA | International Dispensary Association |
| IDSA | Infectious Diseases Society of America |
| LTBI | Latent tuberculosis infection |
| MDR TB | Multidrug-resistant tuberculosis |
| PPD | Purified protein derivative |
| QFT-G | QuantiFERON®-TB Gold test |
| TB | Tuberculosis |
| TST | Tuberculin skin test |
| WHO | World Health Organization |

# APPENDIX B DEFINITIONS

**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 a smear- and/or culture-positive pulmonary tuberculosis case. Contacts exposed in this fashion to persons with smear- or culture-positive pulmonary tuberculosis are at increased risk of infection with *M. tuberculosis*.

**Directly observed therapy (DOT)** – adherence-enhancing strategy in which a health-care worker or other trained person watches a patient swallow each dose of medication. Directly observed therapy is the standard care for all applicants with tuberculosis disease.

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

**Extrapulmonary tuberculosis** – tuberculosis disease in any part of the body other than the lungs (e.g., kidney, spine, or lymph nodes). The presence of extrapulmonary disease does not exclude pulmonary tuberculosis disease. Disease of the lung parenchyma may occur concurrently with pleural tuberculosis, and the parenchymal lung disease may not be apparent on chest radiograph due compression of affected lung tissue by pleural fluid.

**Infection with *M. tuberculosis*** – in some persons who are exposed to and who inhale *M. tuberculosis* bacteria, the bacteria are not promptly cleared by respiratory defense systems and the bacteria multiply and are spread throughout the body, thereby infecting the exposed person. In most persons who become infected, the body is able to fight the bacteria to stop the bacteria from growing, further establishing a latent state. In latent infection, the bacteria are inactive, but they remain alive in the body and can become active later. In other persons, the infection with *M. tuberculosis* can progress to tuberculosis disease more promptly. *M. tuberculosis* infection encompasses both latent tuberculosis infection and tuberculosis disease.

**Latent tuberculosis infection (LTBI)** – infection with *M. tuberculosis* without symptoms or signs of disease manifested.

**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.

**Pulmonary tuberculosis** – tuberculosis disease that occurs in the lung parenchyma, usually producing a cough that lasts >3 weeks. For the purpose of this document, pulmonary tuberculosis refers to both disease of the lung parenchyma and laryngeal tuberculosis

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

**Pre-departure screening evaluations** – the medical evaluation performed within 3 weeks of departure for applicants with equivocal results (e.g., findings suggestive of tuberculosis on medical history, physical exam, or CXR, but do not have positive sputum smears or positive cultures). These applicants should have an evaluation consisting of medical history, physical exam, CXR, and three sputum specimens for AFB microscopy (but no cultures required) within 3 weeks prior to departure.

**Successfully completed tuberculosis therapy** – Therapy for tuberculosis disease taken for the full duration of therapy, including the total number of recommended doses within the appropriate time frame per ATS/CDC/IDSA Guidelines.

**Tuberculosis disease** – condition caused by infection with a member of the *M. tuberculosis* complex that has progressed to causing clinical (manifesting symptoms or signs) or subclinical (early state of disease in which signs or symptoms are not present, but other indications of disease activity are present) illness. The bacteria can attack any part of the body, but disease is most commonly found in the lungs (pulmonary tuberculosis). Pulmonary tuberculosis disease can be infectious, whereas extrapulmonary disease is not infectious, except in rare circumstances. When the only clinical finding is specific chest radiographic abnormalities, the condition is termed "inactive tuberculosis" and can be differentiated from active tuberculosis disease, which is accompanied by symptoms or other indications of disease activity.

# APPENDIX C SPUTUM COLLECTIONS

**Sputum Collection**

- Sputum specimens of 5 – 10 mL
- Preferably early morning specimens
- Three specimens must be collected at least 24 hours apart, preferably on consecutive days
- Should be directly observed
- Applicants should rinse their mouths with purified water before providing a sputum specimen.

**Sputum Specimen Transport**

- Samples should be transported to the laboratory promptly
- If not transported within 1 hour, samples should be refrigerated (but not frozen)
- Ideally, specimens received in the laboratory should be processed within 24 hours of receipt
- Salivary specimens are unacceptable. The collection of a true sputum specimen is of critical importance if the organism is to be isolated.

**Sputum Specimen Processing**

- Sputum specimens should undergo centrifugation before smears are performed.

**Use of Induced Sputum**

- For patients who have difficulty producing sputum, there are several methods of obtaining a specimen. Inhalation of an aerosol of sterile hypertonic saline (3% – 15%), usually produced by an ultrasonic nebulizer, can be used to stimulate the production of sputum. Even though aerosol-induced specimens may appear thin and watery, they should be processed. **The specimen should be clearly labeled as "induced sputum" so it will not be discarded by the laboratory as an inadequate specimen.** Even when alternative methods are used, three specimens are required at least 24 hours apart, preferably on consecutive days.
- Sputum induction can be used for children as young as 3 years of age.
- A gastric aspirate specimen can be used for all ages and may be especially helpful in young children.

# APPENDIX D CULTURES

For specific guidance regarding the performance of cultures for mycobacteria, refer to WHO guidance on laboratory standards (http://www.phppo.cdc.gov/dls/ila/TB_Toolbox.aspx).

**Duration of Culture and Reporting Times**

- Specimens reported as negative should be cultured for a minimum of 6 weeks, with a final report produced within 8 weeks of collection.
- Positive cultures need to be reported within 8 weeks of sputum collection.

# APPENDIX E ADDITIONAL INSTRUCTIONS FOR LARGE REFUGEE RESETTLEMENTS

The following instructions apply for refugees being resettled to the United States. In refugee emergencies, tuberculosis may not be addressed in this manner.

### Refugee populations

Refugees are commonly reported to have elevated rates of tuberculosis. Because many refugees live in large camps that may have crowded living conditions, the potential exists for outbreaks of tuberculosis. Failure to appropriately screen refugees in a timely manner and failure to perform contact investigations can result in refugees with tuberculosis disease remaining undetected which can lead to the development of outbreaks. Extremely elevated rates of tuberculosis and tuberculosis outbreaks may cause refugee movement to be stopped (while control measures are implemented). Moreover, elevated rates of tuberculosis or tuberculosis outbreaks among refugees have the potential to stigmatize these groups and make successful resettlement to the United States more difficult.

### Chest radiographs

Chest radiographs should be performed in close proximity to the medical screening. Documentation of the results for the chest radiographs should be available within 1 week from the time the CXR was performed.

### Contact investigations

When cases of tuberculosis are newly diagnosed, contacts should be identified and screened for tuberculosis disease within 2 weeks of diagnosis of the potential source case.

### Isolation of refugees with tuberculosis

To minimize transmission to others, refugees with smear-positive tuberculosis should be relocated to an isolation area until sputum smears become negative.

### Waivers

The United States is responsible for the health of refugees accepted into the United States Resettlement Program. To ensure adequate care for refugees, attempts should be made to quickly resettle children with tuberculosis disease and refugees with difficult clinical courses.

# APPENDIX F TUBERCULOSIS CLASSIFICATION COVER SHEET

| | | | / / |
|---|---|---|---|
| **Last name** | **First name** | **Alien Number** | **Birth Date** (mm/dd/yyyy) |

*Check all applicable classifications and subcategories*[*]

☐ **No TB Classification**

☐ **Class A TB with waiver**

☐ **Class B1 TB, Pulmonary**
- ☐ No treatment
- ☐ Completed treatment (check all that apply)
  - ☐ Initial smear positive
  - ☐ Initial culture positive
  - ☐ Pre-treatment culture and DST results performed/available
  - ☐ Pre-treatment culture and/or DST results not performed/available

☐ **Class B1 TB, Extrapulmonary** Anatomic site of disease: _____
- ☐ No treatment
- ☐ Current treatment
- ☐ Completed treatment

☐ **Class B2 TB, LTBI Evaluation**

☐ TST conversion

- ☐ TST ≥10 mm (or ≥5 if HIV positive): ___ mm induration
  - ☐ Not started on LTBI treatment
  - ☐ Currently on LTBI treatment (*medications*): _____
  - ☐ Completed LTBI treatment (*medications*): _____

☐ **Class B3 TB, Contact Evaluation**

TST Result: ___mm induration
- ☐ Not started on preventive treatment
- ☐ Currently on preventive treatment (*medications*): _____
- ☐ Completed preventive treatment (*medications*): _____

Source case: Name _____
Alien Number _____
Relationship to contact _____

Date contact ended: (mm/dd/yyyy) ___/___/___

Type of source case TB (mark only one):
- ☐ Pansusceptible TB
- ☐ MDR TB (resistant to at least INH and rifampin)
- ☐ Drug-resistant TB other than MDR TB
- ☐ Culture negative
- ☐ Culture results not available

| | | / / |
|---|---|---|
| **Name of Panel Physician** | **Signature of Panel Physician** | **Date** (mm/dd/yyyy) |

[*]Applicants may have more than one designated classification, e.g., they may be Class B1 Extrapulmonary, Class B2 TB, LTBI Evaluation, and Class B3 TB, Contact Evaluation.

# Index