

CDC IMMIGRATION REQUIREMENTS:

Technical Instructions for Tuberculosis Screening and Treatment



Table of Contents

Preface	iii
Tuberculosis Screening	1
Tuberculosis Screening Results and Travel Clearance.....	5
Tuberculosis Treatment.....	9
Waivers.....	11
Tuberculosis Treatment Monitoring.....	12
Contacts of Tuberculosis Cases.....	13
Pre-departure Tuberculosis Classifications and Descriptions	15
Documentation	16
APPENDIX A Glossary of Abbreviations	17
APPENDIX B Definitions.....	18
APPENDIX C Sputum Collections.....	20
APPENDIX D Cultures	21
APPENDIX E Additional Instructions for Large Refugee Resettlements	22
APPENDIX F Pre-departure TB Classification Cover Sheet	23
Index.....	24

Figures

Figure 1: Tuberculosis screening medical examination for applicants.	2
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Tables

Table 1: Tuberculosis screening results,* travel clearance, and actions.	6
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Preface

The medical screening for tuberculosis among persons overseas applying for U.S. immigration status and non-immigrants 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 404-639-4467.

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 a tuberculosis case.

All applicants 6 months of age or older require screening with medical history, physical examination, and chest radiograph.

All applicants 6 months of age through 5 years of age require screening to include a tuberculin skin test.

All applicants less than 6 months of age require a physical examination and history from a parent or responsible adult who knows the child best.

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

A complete screening medical examination for tuberculosis consists of a medical history, physical examination, chest radiography, determination of immune response to *Mycobacterium tuberculosis* antigens (i.e., tuberculin skin testing [TST] for applicants ≥ 6 months and ≤ 5 years of age), and laboratory testing for human immunodeficiency virus (HIV) infection (for applicants ≥ 15 years of age) and *M. tuberculosis* (when required,

Figure 1).

Pulmonary tuberculosis is disease that involves the lung parenchyma, and is often infectious (i.e., contagious [determined by sputum smear examination for acid-fast bacilli 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.

Technical Instructions for Panel Physicians

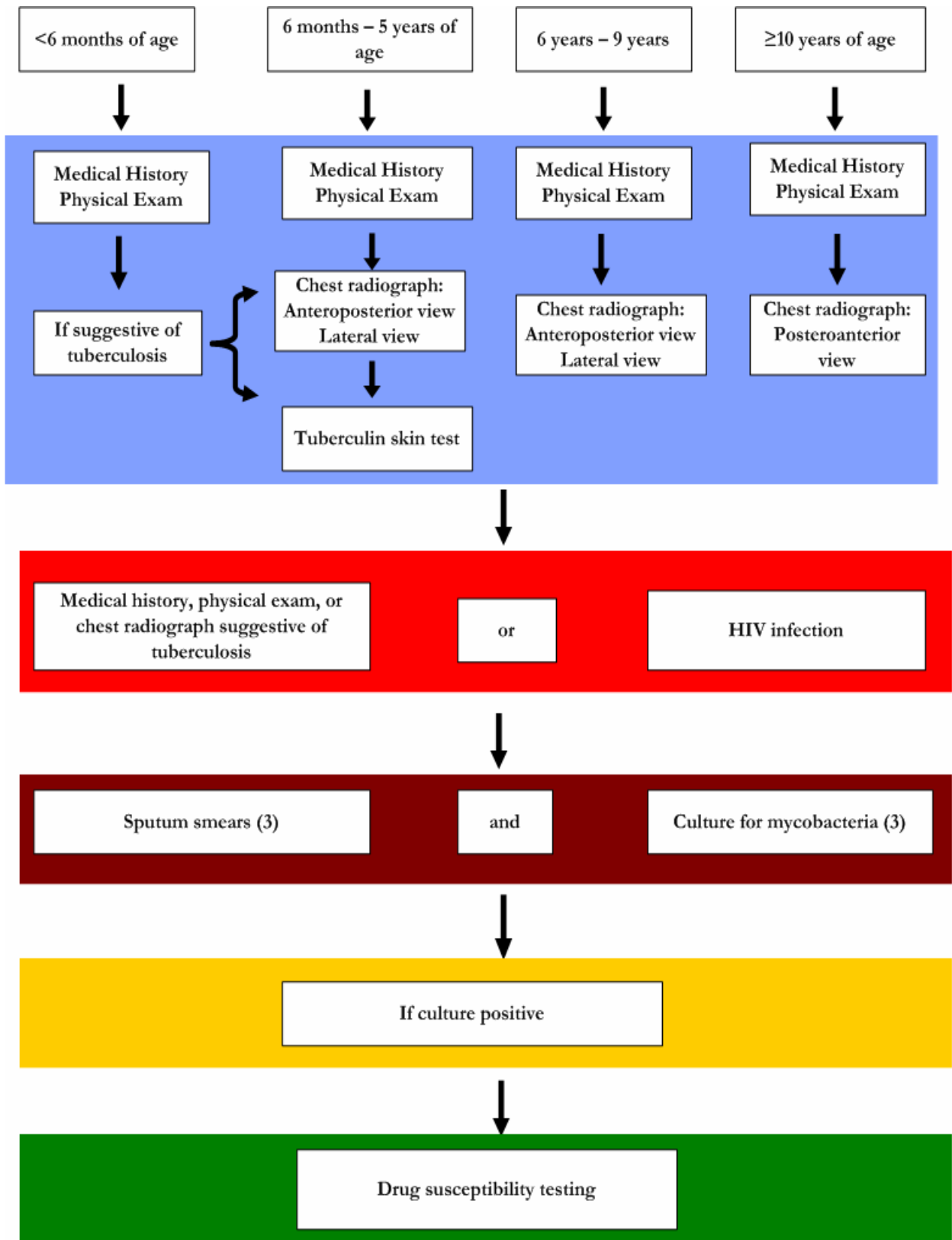


Figure 1: Tuberculosis screening medical examination for applicants.

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 >3 weeks, dyspnea, weight loss, fever, or hemoptysis); prior treatment suggestive of tuberculosis; 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, BCG vaccination, and prior chest surgery.

Chest Radiography

Chest radiography (CXR) should consist of standard anteroposterior views and lateral view for all applicants 6 months through 9 years of age and a standard posteroanterior view for all applicants 10 years of age and older. Women who are pregnant or possibly pregnant will need to provide consent for the CXR and may defer the CXR and their entire evaluation until after delivery. Pregnant women receiving chest radiographs should be provided abdominal and pelvic protection with double layer, wrap around lead shields. 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.

Immune Response to *M. tuberculosis* Antigens

- Determination of immune response to *M. tuberculosis* antigens should be performed by placing a TST as an adjunct to evaluate children ages 6 months through 5 years for tuberculosis disease. Purified protein derivative (PPD [equivalent to 5TU PPD-S]) should be administered intradermally by the Mantoux method. Exceptions include children with written documentation from a physician of previous tuberculosis or where 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. Currently, 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 3 sputum specimens, which 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 (Appendix B, Appendix C). Positive *M. tuberculosis* cultures shall undergo drug susceptibility testing for isoniazid, rifampin, ethambutol, pyrazinamide, and streptomycin. Panel physicians must have access to culture results within 8 weeks of collection.

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.

Tuberculosis Screening Results and Travel Clearance

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

Travel clearances are valid for 6 months from the time the evaluation is complete for applicants with no TB Classification or only Class B2 TB or B3 TB. Travel clearances are valid for 3 months from the time the evaluation is complete for applicants who are Class B1 TB.

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 overseas 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 infected applicants 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 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]).

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. Table 1 lists screening results and required actions for those results.

Technical Instructions for Panel Physicians

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	6 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.

* The evaluation for tuberculosis disease in children ages 6 months through 5 years includes TST; 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. If the applicant is determined to not have tuberculosis disease, the applicant should have a pre-departure evaluation for tuberculosis disease consisting of medical history, physical exam, CXR, and three sputum specimens for AFB microscopy (but no cultures required) within 3 weeks prior to departure. Applicants determined to have tuberculosis disease on the basis of clinical judgment (i.e., are smear and culture negative) should not begin overseas tuberculosis treatment unless the applicant would be harmed by waiting to start therapy after U.S. immigration; these applicants should also have a pre-departure evaluation for tuberculosis disease consisting of medical history, physical exam, CXR, and three sputum specimens for AFB microscopy (but no cultures required) within 3 weeks prior to departure. 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. In addition, the applicant should be evaluated with medical history, physical exam, CXR, and three sputum specimens for AFB microscopy (but no culture required) within 3 weeks prior to departure.

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 ≤5 years of age) can be cleared for travel to the United States (Table 1). Applicants should be assigned a pre-departure tuberculosis classification (No TB Classification, Appendix F).
- Applicants ≤5 years of age who have a TST ≥10 mm and are without HIV infection (if tested), 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 pre-departure tuberculosis classification to receive evaluation for LTBI in the United States (Class B2 TB, LTBI Evaluation).
- Children <6 months of age who have any findings suggestive of tuberculosis on their medical history or physical examination should have chest radiography (anteroposterior and lateral views) performed and three sputum specimens (or alternative specimens such as gastric aspirates) sent to the laboratory for AFB microscopy and culture. These children cannot be cleared for travel until the results of the laboratory investigation are available (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., findings suggestive of tuberculosis on medical history, physical exam, or CXR, but 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. Applicants who are determined not to have tuberculosis disease should have a pre-departure evaluation for tuberculosis disease consisting of medical history, physical exam, CXR, and three sputum specimens for AFB microscopy (but no cultures required) within 3 weeks prior to departure (if evaluation negative, Class B1 TB, Pulmonary).

Technical Instructions for Panel Physicians

- Applicants who have successfully completed therapy for tuberculosis, in addition to the medical screening for all applicants, should also have a medical examination for tuberculosis consisting of medical history, physical exam, CXR, and three sputum specimens for AFB microscopy (but no cultures required) within 3 weeks prior to departure (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 pre-departure tuberculosis classification (Class B1 TB, Extrapulmonary). Efforts should be made to obtain a laboratory confirmed diagnosis. Applicants clinically diagnosed with extrapulmonary tuberculosis should not have treatment begun overseas unless the applicant would be harmed by waiting to start therapy after immigration. Applicants with extrapulmonary disease who are started on therapy prior to departure can 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, including children, diagnosed with tuberculosis disease who are smear and culture negative should not have treatment begun overseas unless the applicant would be harmed by waiting to start therapy after immigration.

**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 completed by panel physicians using these standards or by programs identified by the Division of Global Migration and Quarantine.

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.

Treatment of tuberculosis, both pulmonary and extrapulmonary, should be administered following DOT policies and practices.

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. Panel physicians should not begin overseas tuberculosis treatment on these patients unless the applicant would be harmed by waiting to start therapy after U.S. immigration. These

Technical Instructions for Panel Physicians

applicants should have a pre-departure evaluation for tuberculosis disease consisting of medical history, physical exam, CXR, and three sputum specimens for AFB microscopy (but no cultures required) within 3 weeks prior to departure.

Treatment of U.S. applicants should be administered consistent with the 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).

Consultations on any tuberculosis case will be coordinated by the Division of Global Migration and Quarantine on an individual basis. The Division of Global Migration and Quarantine will access subject matter expertise with the Division of Tuberculosis Elimination (DTBE). Treatment of drug-resistant and multidrug-resistant tuberculosis (MDR TB) should be done by or in close consultation with an expert in the management of such cases and in coordination with the Division of Global Migration and Quarantine. The Division of Global Migration and Quarantine should also be contacted to facilitate consultations with DTBE and the Global AIDS Program (GAP) for situations such as diagnosis and treatment of children, pregnant women, or HIV-infected patients receiving highly active retroviral therapy. 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, the Division of Global Migration and Quarantine 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 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 that 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.

One sputum smear should be collected and submitted for AFB microscopy and mycobacteria culture at the end of therapy, regardless of initial clinical, CXR, or laboratory findings.

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:** one sputum smear should be collected and submitted for AFB microscopy and mycobacteria culture once a month during therapy until cultures are negative for 2 consecutive months.
- **Resistant to only one drug (including resistant to only isoniazid or rifampin):** one sputum smear should be collected and submitted for AFB microscopy and mycobacteria culture once a month during therapy until cultures are negative for 2 consecutive months.
- **Resistant to more than one drug but susceptible to isoniazid or rifampin (drug resistant but not MDR TB):** one sputum smear should be collected and submitted for AFB microscopy and mycobacteria culture once a month during therapy until cultures are negative for 2 consecutive months.
- **MDR TB (resistant at least to both isoniazid and rifampin):** one sputum smear should be collected and submitted for AFB microscopy and mycobacteria culture once a month during the entire course of therapy.
- **No drug susceptibility testing results (culture negative):** one sputum smear should be collected and submitted for AFB microscopy and mycobacteria culture once a month during therapy.

Contacts of Tuberculosis Cases

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

All contacts of smear or culture positive pulmonary tuberculosis cases that are continually exposed should be evaluated with a medical history, physical exam, and CXR at 3 month intervals for the first 6 months of continual exposure and again every 6 months until exposure ends. When exposure ends, the contact should be evaluated 8 weeks after last exposure.

Contacts who have clinical findings or CXR findings suggestive of tuberculosis should provide at least three sputum specimens for AFB microscopy and mycobacteria culture.

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 pre-departure tuberculosis classification (Appendix F).

Applicants who are contacts to a case with MDR TB or INH-resistance should be evaluated with a medical history, physical exam, and CXR every 3 months for 6 months, then every 6 months, until 24 months after end of estimated exposure. The contact may travel at any point when tuberculosis disease has been ruled out and should be assigned a pre-departure tuberculosis classification (Appendix F).

If an applicant has been identified as a contact to a tuberculosis case, more than 8 weeks have elapsed since the last exposure, and evaluation for tuberculosis was negative at least 8 weeks after last exposure, the applicant should not be designated as a contact on the pre-departure tuberculosis classification cover sheet.

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).

Technical Instructions for Panel Physicians

Children <4 years of age and applicants with impaired immunity (e.g., HIV infection) who are family or household 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 tuberculin skin test 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 ≥ 6 months and ≤ 5 years of age 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 pre-departure tuberculosis classification 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.

Children <4 years of age and applicants with impaired immunity (e.g., HIV infection) who are family or household contacts of a pulmonary tuberculosis case with isoniazid resistance (including MDR TB) and who have a negative evaluation for tuberculosis should not be given overseas preventive therapy. If not continually exposed, they should receive an evaluation for tuberculosis (i.e., medical history, physical exam, CXR, and tuberculin skin test [if ≥ 6 months and ≤ 5 years of age]) 8 weeks after last exposure. If continually exposed, these children should be evaluated (i.e., medical history, physical exam, CXR, and tuberculin skin test for tuberculosis [if ≥ 6 months and ≤ 5 years of age]) at 3-month intervals for the first 6 months, then every 6 months until exposure ends (when exposure ends, the contact should be evaluated 8 weeks after last exposure).

Pre-departure Tuberculosis Classifications and Descriptions

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

The pre-departure 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, 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. The anatomic site of infection should be documented.

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.

Class B3 TB, Contact Evaluation

Applicants who are a contact of a known tuberculosis case. The size of the applicant's TST reaction should be documented, if performed. 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 pre-departure tuberculosis classification for each applicant and complete the Pre-departure 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 name of product, expiration date, amount administered, and the type of product used (i.e., 5TU PPD-S equivalent or 2TU of RT 23).
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 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 (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
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 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 suspected or confirmed tuberculosis disease. 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 to 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 the majority of persons who become infected, the body is able to fight the bacteria to stop the bacteria from growing, further establishing a latent state. 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 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 are required at least 24 hours apart, preferably on consecutive days
- Should be directly observed

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.** 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 at 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 specimen receipt.

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 re-located to an isolation area until sputum smears become negative while on treatment.

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. When necessary, Class A waivers should be vigorously pursued for these refugees.

APPENDIX F PRE-DEPARTURE TB CLASSIFICATION COVER SHEET

			/ /
Last name	First name	Alien Number	Birth Date (mm/dd/yyyy)
<i>Check all applicable classifications and subcategories*</i>			
<input type="checkbox"/> No TB Classification			
<input type="checkbox"/> Class A TB with waiver			
<input type="checkbox"/> Class B1 TB, Pulmonary <input type="checkbox"/> No treatment <input type="checkbox"/> Completed treatment <input type="checkbox"/> Initial smear positive <input type="checkbox"/> Initial culture positive <input type="checkbox"/> Pre-treatment culture and DST results performed/available <input type="checkbox"/> Pre-treatment culture and/or DST results not performed/available			
<input type="checkbox"/> Class B1 TB, Extrapulmonary Anatomic site of disease: _____ <input type="checkbox"/> No treatment <input type="checkbox"/> Current treatment <input type="checkbox"/> Completed treatment			
<input type="checkbox"/> Class B2 TB, LTBI Evaluation <input type="checkbox"/> TST ≥ 10 mm (or ≥ 5 if HIV positive): ___ mm induration <input type="checkbox"/> Not started on LTBI treatment <input type="checkbox"/> Currently on LTBI treatment (<i>medications</i>): _____ <input type="checkbox"/> Completed LTBI treatment (<i>medications</i>): _____			
<input type="checkbox"/> Class B3 TB, Contact Evaluation TST Result: ___mm induration <input type="checkbox"/> Not started on preventive treatment <input type="checkbox"/> Currently on preventive treatment (<i>medications</i>): _____ <input type="checkbox"/> Completed preventive treatment (<i>medications</i>): _____ Source case: Name _____ Alien Number _____ Relationship to contact _____ Type of source case TB (mark only one): <input type="checkbox"/> Pansusceptible TB <input type="checkbox"/> MDR TB (resistant to at least INH and rifampin) <input type="checkbox"/> Drug-resistant TB other than MDR TB <input type="checkbox"/> Culture negative <input type="checkbox"/> Culture results not available			
		Date contact ended: (mm/dd/yy) ___ / ___ / ___	
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

- ATS/CDC/IDSA Guidelines, 9. *See also* tuberculosis treatment
- BCG (Bacille Calmette-Guérin) Vaccine.
 - prior receipt of, 3, 4. *See also* tuberculosis screening
- chest radiographs, 3
- children
 - chest radiography, recommendations for, 3, 7
 - family/household contacts of TB cases, 13, 14
 - immune response to *M. tuberculosis* antigens, 4
 - large refugee resettlements, E-1
 - medical history, 3
 - sputum specimens, collection of, 5, C-1
 - tuberculin skin testing (TST), 7, 3
 - tuberculosis screening requirements, 1
 - treatment after tuberculosis diagnosis, 9, 10
- contacts of tuberculosis cases, 13
 - directly observed preventive therapy (DOPT), 13
 - MDR TB or INH-resistant TB, 13, 14
 - treatment of children, less than four years old, 13, 14
 - treatment prior to U.S. immigration, 13
- Department of State forms, 16. *See also* documentation.
- Division of Global Migration and Quarantine
 - documentation sent to, 16
 - TB treatment assistance provided by, 9
 - treatment consultation with, 10
- DGMQ. *See* Division of Global Migration and Quarantine
- documentation, 16
 - chest radiography findings, 16
 - clinical course, 16
 - cultures for mycobacteria, 16
 - Department of State (DS) form, 16
 - DS-2053, 16
 - DS-3024, 16
 - DS-3025, 16
 - DS-3026, 16
 - DOT regimen, 16
 - drug susceptibility test results, 16
 - pre-departure screening, 16
 - pre-immigration medical screening, 16
 - sputum smears, 16
- drug-resistant tuberculosis
 - treatment of, 10
 - treatment monitoring, 12
 - use of fluoroquinolones, 5
- Francis J. Curry National Tuberculosis Center, 10. *See also* tuberculosis treatment.
- HIV. *See* Human Immunodeficiency Virus
- Human Immunodeficiency Virus (HIV)
 - applicants with, 7
 - applicants without, 7
 - infected contacts of TB cases, 13, 14
 - laboratory testing for, 1, 4
 - treatment of infected applicants, 10
 - waivers for infected applicants, 11
- isoniazid, 12
 - contacts, using, 13-14
 - directly observed preventive therapy (DOPT), 13
 - travel clearance, 14
 - treatment for family and household tuberculosis treatment monitoring of, 12
- large refugee resettlement
 - instructions for, E-1
- latent tuberculosis infection (LTBI)
- latent tuberculosis infection (continued)

- detection of, 4
 - evaluation for, 7
 - pre-departure classification and description, 15
- multi-drug resistant tuberculosis (MDR TB)
 - treatment, 10
 - treatment monitoring, 12. *See also* Division of Global Migration and Quarantine
- pre-departure tuberculosis classifications and descriptions, 15
 - Class A TB with waiver, 15
 - Class B1 TB, extrapulmonary, 15
 - Class B1 TB, pulmonary, 15
 - no treatment, 15
 - treatment completed, 15
 - Class B2 TB, LTBI Evaluation, 15
 - Class B3 TB, contact evaluation, 15
 - no tuberculosis classification, 15
- pregnant women
 - chest radiographs, 3
 - tuberculosis treatment, 10
- rifampin
 - drug susceptibility testing, 4
 - TB resistant to, 12
 - TB susceptible to, 12
- TST. *See* tuberculin skin test
- tuberculin skin test (TST)
 - after exposure to disease, 13
 - during continual exposure to, 14
 - reaction and classification, 15
 - required screening, 1
- tuberculosis screening, 1
 - antigens, 4
 - Latent M. tuberculosis infection (LTBI), 4,
 - Mantoux method, 4
 - purified protein derivative (PPD), 4
 - QuantiFERON®-TB Gold (QFT-G), 4
 - tuberculin skin test (TST), with, 4
 - chest radiography (CXR), 3,
 - children, 3
 - contacts of TB patients, evaluation of, 13, 14
 - pelvic shielding, 3
 - pre-departure classification, 15
 - pre-departure evaluation, 10
 - pregnant women, for, 3
 - screening results and travel clearance, as part of, 5-7
 - treatment monitoring, 12
 - immune response to M. tuberculosis
 - laboratory testing, 4
 - acid-fast bacilli (AFB) microscopy, for, 4
 - HIV infection, for, 4
 - mycobacteria, for, 4
 - sputum specimens, 4
 - medical history, 3
 - Bacille Calmette-Guérin (BCG) vaccine 3,4,
 - children, 3
 - family contact, 3
 - previous history, 3
 - risk factors, 3
 - physical exam, 3
 - pertinent elements, 3
 - scars of scrofula, 3
- tuberculosis screening results and travel clearance, 5
 - AFB microscopy, positive for, 7
 - applicants with laryngeal tuberculosis, 8
 - bacterial infections, treatment of, 7
 - completion of tuberculosis therapy, 7
 - extrapulmonary tuberculosis diagnosis, 8
 - equivocal results, 7
 - fluoroquinolones, use of, 5
 - HIV positive applicants, for, 7
 - no clinical findings of tuberculosis, 7
 - no tuberculosis disease, 7
 - positive Mycobacterium cultures, 7
 - respiratory infections, treatment of, 5
 - screening results and travel clearance, 7
 - tuberculosis present, 7
 - with negative sputum smears, 7
- tuberculosis treatment, 9

- American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America (ATS/CDC/IDSA) guidelines, 9
- directly observed therapy (DOT), 9
- drug-resistant and multi-drug resistant (MDR), consultation of, 10
- drug susceptibility testing results, based on, 10
- first-line and second-line drugs, 9
- Francis J. Curry National Tuberculosis Center, “Drug-resistant tuberculosis: a survival guide for clinicians”, 10
- Global Drug Facility (GDF), 9
- International Dispensary Association, (IDA, Amsterdam), 9
- negative sputum smears and negative cultures, 9
- non-compliant patients (patients refusing treatment), 9
- panel physician’s obligation, 9, 10
- quality assured drugs, 9
- WHO Green Light Committee, 9

tuberculosis treatment monitoring, 12

- drug-resistant but not multi-drug resistant, 12

tuberculosis treatment monitoring (continued)

- drug-susceptible, 12
- multi-drug resistant tuberculosis, (MDR TB) 12
- no drug susceptible, 12
- one drug resistant, 12

United States (U.S.) Embassy

- documentation sent to, 16

waivers, 11

- Class A waivers, exceptional situations, 11
- laryngeal tuberculosis, 11
- prior notification and approval, , 11
- pulmonary tuberculosis, 11