Appendices

Appendix I-A

Dosages for Primary Medications Used in the Treatment of Tuberculosis

Drug ***Route of Administration*** **Mode of Action**	**Daily Dose [Max]**	**3 Times a Week Dose [Max]**	**2 Times a week Dose [Max]**	**Major Adverse Reactions***
Isoniazid[1] *Oral/Intramuscular* Bactericidal	Children: 5-10 mg/kg[2] Adults: 5 mg/kg [300mg]	Children: 20 mg/kg Adults: 10 mg/kg (range 8-12 mg/kg) [900mg]	Children: 20 mg/kg Adults: 15 mg/kg (range 13-17 mg/kg) [900mg]	Hepatic enzyme elevations, hepatitis, rash, peripheral neuropathy, CNS effects, increased phenytoin levels, possible interaction with disulfiram (Antabuse®)
Rifampin[1] *Oral/Intravenous* Bactericidal	Children: 10-20 mg/kg[3] Adults: 600 mg (range 8-12 mg/kg) [600mg]	Children: 10-20 mg/kg Adults: 600 mg (range 8-12 mg/kg) [600mg]	Children: 10-20 mg/kg Adults: 600 mg (range 8-12 mg/kg) [600mg]	Hepatic enzyme elevations, hepatitis, rash, fever, thrombocytopenia, influenza-like syndrome, reduced levels of many drugs (including methadone), warfarin, hormonal forms of contraception, oral hypoglycemic agents, theophylline, dapsone, ketoconazole, PIs and NNRTIs.
Rifabutin[4] *Oral* Bactericidal	Children: 5 mg/kg Adults: 5 mg/kg [300mg]			Rash; hepatitis, fever, neutropenia, thrombocytopenia, reduced levels of many drugs, including PIs, NNRTIs, dapsone, ketoconazole and hormonal forms of contraception.
Rifapentine[5] *Oral* Bactericidal				Same as rifampin
Pyrazinamide[1] *Oral* Bacteriostatic	Children: 25 mg/kg (range 20-30 mg/kg) Adults: 25 mg/kg (range 20-30 mg/kg) [2 g for C and A]	Children: 35 mg/kg (range 30-40 mg/kg) Adults: 35 mg/kg (range 30-40 mg/kg) [3 g for C and A]	Children: 50 mg/kg (range 40-60 mg/kg) Adults: 50 mg/kg (range 40-60 mg/kg) [3.5 g for C and A]	Gastrointestinal (GI) upset, hepatotoxicity, hyperuricemia, gout (rarely), arthralgias, rash
Ethambutol *Oral* Bacteriostatic	Children: 20 mg/kg (range 15-25 mg/kg) [1.5 g] Adults: 15-25 mg/kg [2.0 g]	Children: 30 mg/kg (range 25-35 mg/kg) Adults: 30 mg/kg (range 25-35 mg/kg) [2.8 g]	Children: 40-50 mg/kg [2.5 g] Adults: 45 mg/kg (range 40-50 mg/kg) [3.6 g]	Decreased red-green color discrimination, decreased visual acuity, skin rash
Streptomycin *Intramuscular/* *Intravenous* Bactericidal	Children: 15-30 mg/kg Adults: 15 mg/kg [1,000 mg]	Children: 15 mg/kg Adults: 15 mg/kg [1,000 mg]	Children: 15 mg/kg Adults: 15 mg/kg [1,000 mg]	Auditory toxicity, renal toxicity, hypokalemia, hypomagnesemia

Abbreviations: HAART = highly active antiretroviral therapy, NNRTI = non-nucleoside reverse transcriptase inhibitor, PI = protease inhibitor

* All toxicities are not listed here. Full prescribing information should be checked in the package insert or pharmacology texts.
Use of brand names is for informational purposes only and does not imply endorsement by the NYC Department of Health and Mental Hygiene.

[1] An isoniazid/rifampin combination tablet (Rifamate®)* containing 150 mg of isoniazid and 300 mg of rifampin, and an isoniazid/rifampin/pyrazinamide combination (Rifater®)* containing 50 mg of isoniazid, 120 mg of rifampin, and 300 mg of pyrazinamide are available and should be used whenever patients are NOT on directly observed therapy.

Recommended Regular Monitoring	Comments
• Monthly clinical evaluation • Liver function tests[6]	• Vitamin B_6 (pyridoxine) 25 mg/day may decrease peripheral neuritis and central nervous system effects and should be used in patients who are abusing alcohol, pregnant, breastfeeding infants on isoniazid, malnourished, or who have HIV infection, cancer, chronic renal or liver disease, diabetes, or pre-existing peripheral neuropathy. • Aluminum-containing antacids reduce absorption. • Drug interactions with several agents
• Monthly clinical evaluation • Complete blood cell count including platelets and liver function tests as indicated[6]	• Orange discoloration may occur in contact lenses and body secretions such as tears and urine. • Patients receiving methadone will need their methadone dosage increased, by an average of 50%, to avoid opioid withdrawal. • Interaction with many drugs leads to decreased levels of the co-administered drug. • May make glucose control more difficult in people with diabetes. • Contraindicated for patients taking most PIs and NNRTIs. • Patients should be advised to use barrier contraceptives while on rifampin.
• Monthly clinical evaluation • Complete blood cell count including platelets and liver function tests as indicated[6]	• Orange discoloration may occur in contact lenses and body secretions, urine, tears and contact lenses. • Can be used daily, or in 2 or 3 times per week dosing schedule. [See Table III-3, p. 55 for treatment of HIV-infected persons.] • If taken concurrently with PIs or NNRTIs, adjust dose of rifabutin and monitor for decreased antiretroviral activity and for rifabutin toxicity. • Contraindicated for patients taking single PI, ritonavir/saquinavir or delaviridine based HAART regimen. • Methadone dosage generally does not need to be increased. • Patients should be advised to use barrier contraceptives while on rifabutin.
• Monthly clinical evaluation • Complete blood cell count including platelets and liver function tests as indicated[6]	• Same as rifampin. • Rifapentine 600 mg should be administered with isoniazid 900 mg once a week only in the continuation phase of treatment of non-cavitary drug-susceptible pulmonary TB in HIV-negative patients 12 years of age and older, who are not pregnant.
• Monthly clinical evaluation • Liver function test as indicated[6]	• May complicate management of diabetes mellitus. • Hyperuricemia can be used as indicator of compliance. • Treat increased uric acid only if symptomatic. • Allopurinol increases level of pyrazinamide by inhibiting xanthine oxidase resulting in failure of allopurinol to lower serum uric acid.
• Monthly clinical evaluation • Check color vision and visual acuity monthly	• Optic neuritis may be unilateral; check each eye separately. If possible, avoid in children too young to undergo vision testing. • If patient develops visual complaints, refer for prompt ophthalmologic evaluation. May need to discontinue ethambutol while awaiting evaluation.
• Monthly clinical evaluation • Audiometry, renal function, electrolytes, including magnesium	• Ultrasound and warm compresses to injection site may reduce pain and induration.

[2] World Health Organization (WHO), International Union Against TB and Lung Disease (IUATLD), and British Thoracic Society (BTS) recommend 5 mg/kg in children; Centers for Disease Control and Prevention (CDC)/American Thoracic Society (ATS), Infectious Disease Society of America (IDSA) and the American Academy of Pediatrics (AAP) recommend 10-20 mg/kg.
[3] WHO, IUATLD, and BTS recommend 10 mg/kg in children; CDC/ATS and the AAP recommend 10-20 mg/kg.
[4] Not FDA-approved for the treatment of TB
[5] Rifapentine should not be used in patients who are HIV-infected.
[6] Liver function tests are indicated if baseline is abnormal or patient has risk factors for toxicity.

Appendix I-B

Dosages for Reserve Medications Used in the Treatment of Tuberculosis*

Drug *Route of Administration* Mode of Action	Daily Dose [Max]	Major Adverse Reactions*	Recommended Regular Monitoring	Comments
Capreomycin *Intramuscular/Intravenous* Bactericidal	Children: 15–30 mg/kg Adults: 15 mg/kg [1000 mg]	Auditory, vestibular, and renal toxicity, eosinophilia, hypokalemia, hypomagnesemia	• Monthly clinical evaluation • Audiometry, renal function, electrolytes, including magnesium	• Ultrasound and warm compresses to injection site may reduce pain and induration.
Cycloserine *Oral* Bacteriostatic	Children: 10–20 mg/kg Adults: 500–1000 mg, divided doses [1000 mg]	Psychosis, seizures, headache, depression, suicide, other CNS effects, rash, increased phenytoin levels	• Monthly clinical evaluation • Assess and monitor mental status	• Increase gradually, checking serum levels. • Pyridoxine hydrochloride (vitamin B_6) may decrease CNS effects (use 50 mg for each 250 mg of cycloserine).
Ethionamide *Oral* Bacteriostatic	Children: 15–20 mg/kg Adults: 500–1000 mg, divided doses [1000 mg]	Nausea, vomiting, diarrhea, abdominal pain, bloating, hepatotoxicity, hypothyroidism (especially when administered with PAS), metallic taste	• Monthly clinical evaluation • Liver function tests (if baseline abnormal) • Thyroid function periodically especially if also on para-aminosalicyclic acid	• Antacids/anti-emetics and lying supine for 20 minutes after dose may help tolerance. • Start with 250 mg daily and increase as tolerated.
Kanamycin Amikacin *Intramuscular/Intravenous* Bactericidal	Children: 15–30 mg/kg Adults: 15-22.5 mg/kg [1000 mg]	Auditory toxicity, renal toxicity, vestibular toxicity (rare), hypokalemia, hypomagnesemia	• Monthly clinical evaluation • Audiometry, renal function, electrolytes, including magnesium	• Ultrasound and warm compresses to injection site may reduce pain and induration.
Levofloxacin** *Oral/Intravenous* Bacteriostatic, possibly bactericidal	Children: 6 months to under 5 years old: 10 mg/kg bid 5 years and older: 10 mg/kg qd. Adults: 500–1000 mg in one dose	Nausea, vomiting, diarrhea, abdominal pain, tremulousness, insomnia, headache, dizziness, lightheadedness, photosensitivity, tendonitis, tendon rupture, possible hypo-and hyperglycemia hypersensitivity	• Monthly clinical evaluation • Monitor blood sugar	• Most active of the fluoroquinolones commonly used for TB (ciprofloxacin, levofloxacin, ofloxacin) • Preferred fluoroquinolone • Our clinical experience shows safety with long term use.
Moxifloxacin** *Oral/Intravenous* Bactericidal	Children: Dose unknown Adults: 400 mg	Similar to levofloxacin	• Monthly clinical evaluation • Monitor blood sugar	• More active than levofloxacin against *M. tb.* • There is little experience with the use of this drug for longer than 14 days. Therefore, data on adverse effects with prolonged use for TB are limited. • Avoid in patients with prolonged QT interval and those receiving class Ia or III antiarrhythmic agents.
Para-aminosalicyclic Acid *Oral* Bacteriostatic	Children: 150 mg/kg Adults: 4 g every 12 h [12g]	Nausea, vomiting, diarrhea, abdominal pain, hypersensitivity, hepatoxicity, hypothyroidism (especially when administered with ethionomide), decreased digoxin levels, increased phenytoin levels, PAS levels decreased by diphenhydramine	• Monthly clinical evaluation • Thyroid function periodically especially if also on ethionamide	• Begin gradually and increase dosage as tolerated. • May cause hemolytic anemia in patients with glucose 6-phosphate dehydrogenase (G-6-PD) deficiency.

Abbreviation: PAS = para-aminosalycilic acid

* All toxicities are not listed here. Full prescribing information should be checked in the package insert or pharmacology texts. Use of brand names is for informational purposes only and does not imply endorsement by the New York City Department of Health and Mental Hygiene.

** Although flouroquinolones are not approved for use in children in most countries, the benefit of treating children with MDRTB with a flouroquinolone may outweigh the risk in many instances.

Appendix I-C

The Use of Antituberculosis Drugs during Pregnancy, Breastfeeding, Tuberculosis Meningitis, and Renal and Hepatic Failure[1]

Drug	Safety in Pregnancy[2]	Safety in Breastfeeding	Central Nervous System Penetration[3]	Dosage in Renal Insufficiency[4]	Dosage in Hepatic Insufficiency
Isoniazid	Has been used safely[5]	Moderately safe	Good (20%-100%)	No change	No change, but use with caution
Rifampin	Has been used safely (isolated reports of malformations)	Safe	Fair (inflamed meninges) (10%-20%)	No change	No change, but use with caution
Rifapentine	Safety not established	No data	Not established	Not established Use with caution	No change, but use with caution
Rifabutin	Use with caution (limited data on safety)	No data	Good (30%-70%)	No change	No change, but use with caution
Pyrazinamide	Recommended by WHO[6] (not by US FDA[7])	Moderately safe	Good (75%-100%) (use with caution)	Decrease dosage/ increase interval (use with caution)	No change, but use with caution
Ethambutol	Has been used safely	Safe	Inflamed meninges only (4%-64%)	Decrease dosage/ increase interval[4]	No change
Aminoglycosides (streptomycin, kanamycin, amikacin)	Avoid[8] (associated with ototoxicity in fetus)	Safe	Poor[9]	Decrease dosage/ increase interval[4,10]	No change
Capreomycin	Avoid[8] (limited data on safety)	No data	Poor	Decrease dosage/ increase interval[10]	No change
Levofloxacin	Do not use (teratogenic in laboratory animals)	Moderately safe	Fair (16%-20%)	Increase interval	No change, but use with caution
Moxifloxacin	Do not use (teratogenic in laboratory animals)	Moderately safe	Fair (5%-10%) Inflamed meninges (50%-90%)	No change, but use with caution	No change, but use with caution, especially with severe hepatic insufficiency
Cycloserine	Use with caution (limited data on safety)	Moderately safe	Good (50%-100%)	Decrease dosage/ increase interval[4]	No change
Ethionamide	Do not use (premature labor, congenital malformations)	No data	Good (100%)	No change, but use with caution	No change, but use with caution
Para-aminosalicyclic acid	Has been used safely	Moderately safe	Inflamed meninges only	No change, but use with caution	No change, but use with caution

[1] This table presents a consensus of published data and recommendations.
[2] As with all medications given during pregnancy, anti-TB medications should be used with extreme caution. The risk of TB to the fetus far outweighs the risk of most medications. Data are limited on the safety of anti-TB medications during pregnancy.
[3] Steroid treatment appears to improve outcome in TB meningitis, particularly in patients with altered mental status.
[4] If possible, monitor serum drug levels of patients with renal insufficiency.
[5] Supplement with pyridoxine hydrochloride (vitamin B_6), 25 mg per day
[6] World Health Organization
[7] Food and Drug Administration
[8] If an injectable medication must be used during pregnancy, streptomycin is the preferred agent if the organism is susceptible.
[9] Has been used intrathecally: efficacy not documented
[10] If possible, avoid aminoglycosides and capreomycin in patients with reversible renal damage.

Appendix I-D

Late Complications of Treated Pulmonary Tuberculosis

Some patients who have been successfully treated for pulmonary tuberculosis (TB) in the past develop symptoms or have abnormalities on a chest X-ray (CXR) that raise the possibility of a recurrence of active TB. However, a few other late complications should be considered in the differential diagnosis in such patients.

Hemoptysis

Bleeding from ruptured bronchial veins. Some individuals with fibrotic residuals of pulmonary TB, such as contracted lobes or segments, residual "open healed" cavities, or localized fibrosis, develop hemoptysis due to bleeding from the old, inactive post-tuberculous lesion. In most cases, the origin of the blood is a ruptured bronchial vein that occurs in rich plexuses in the endobronchial mucosa in such lesions. Hemoptysis often begins during an acute viral respiratory infection. It is usually self-limited, but may be so severe as to require emergency surgical resection.

This cause of hemoptysis can be diagnosed only by ruling out the other causes outlined here, as well as active TB (by obtaining multiple sputum cultures). If sputum cultures are negative, and no other criteria prove active TB, patients with hemoptysis should not be retreated for active TB.

Mycetoma. Healed TB cavities can be colonized by fungi, usually *Aspergillis species*, and evolve into a mass of matted mycelia—a movable, intracavitary "fungus ball." This process is accompanied by the development of vascular granulation tissue in the internal wall of the cavity, which appears on serial CXRs as a progressive thickening of the cavity wall. In some cases, this thickening is evident even before a mycetoma can be visualized. The granulation tissue is the site of bleeding in some individuals with *Aspergillis*-colonized cavities, usually with mycetoma. Some patients experience massive hemoptysis and require an emergency surgical resection of involved tissue or radiological intervention. Others experience chronic or recurrent hemoptysis of lesser amounts.

The diagnosis can be suspected on the basis of characteristic radiological signs, cultural isolation *Aspergillis* from sputum and the presence of serum antibodies, usually against *Aspergillis fumigatus*.

Other causes of hemoptysis. Many conditions unrelated to TB may lead to hemoptysis in patients who were treated for TB in the past. Among these are pneumonia, pulmonary emboli, bronchiectasis, lung abscess and tumors.

Patients with hemoptysis may need further evaluation such as computed tomography (CT) scan of the chest, and pulmonary/ surgical consultation.

Chest Pain

Some patients with successfully treated tuberculous pleural effusions experience chest pain over a period of months or years. Some describe pleuritic pain; others, chronic aching or a burning sensation. Often the cause is not clear. Unless there is a demonstrable recurrence of a pleural effusion on the CXR, treatment for active TB is not indicated. Infrequently, chest pain may be due to a spontaneous pneumothorax caused by the rupture of a bleb, which can evolve in an area of pulmonary scarring related to TB.

Dyspnea

Patients with extensive pulmonary or pleural fibrosis due to healed TB may experience exertional dyspnea. Pulmonary function tests demonstrate a restrictive defect. Except for this cause, the development of dyspnea after successful therapy for TB usually reflects the presence of another, unrelated cause (e.g., chronic obstructive pulmonary disease, asthma, heart disease, anemia).

Recurrence of Cough, Sputum, Fever or Weight Loss

Such symptoms are nonspecific and may occur from a wide variety of respiratory diseases other than TB. Among these are viral, mycoplasmal, bacterial, fungal and other respiratory infections; exacerbations of bronchiectasis or chronic bronchitis; and tumors. In such cases, the reinstitution of anti-TB treatment is not indicated unless cultures are positive for *Mycobacterium tuberculosis* or the CXR suggests recurrent TB.

Clubbed Fingers

Clubbed fingers may be found in individuals with very advanced pulmonary TB and chronic respiratory insufficiency. However, if a patient who has been previously treated for pulmonary TB subsequently develops clubbed fingers, another cause — especially a tumor — should be strongly suspected, even if the CXR has not changed.

Changes in the Appearance of the Chest X-ray

In an individual who has been treated for TB, these changes may reflect a recurrence of active TB, even in the absence of symptoms. However, they could be due to completely different causes, including the following:

Mycetoma. A mycetoma is usually characterized by a thickening of the cavity wall or the presence of an intracavitary mass, often manifesting a "crescent" sign.

Tumor. "Scar" cancer may develop at the site of post-tuberculous fibrosis, or even on the wall of a healed TB cavity. The former usually presents as a new solitary spherical lesion in the lung parenchyma; the latter, as a localized thickening of the cavity wall or as a nonmovable intracavitary mass that can closely resemble a mycetoma.

Endobronchial lesions. Endobronchial lesions that obstruct lobar or segmental bronchi usually lead to an airless, "collapsed" lobe or segment or to chronic organizing pneumonia in the parenchyma distal to the obstruction. Such lobar or segmental lesions should be suspected to be due to a tumor, malignant or benign, or to a foreign body. Appropriate diagnostic investigation should be undertaken.

Fluid level in an emphysematous bleb. Although "open healed" TB cavities are rarely secondarily infected, or the site of fluid levels, emphysematous bullae in the area of healed TB may develop fluid levels, especially after lower respiratory infections. These rarely represent reactivated TB.

Pleural effusion. Recurrent TB infection may present as a pleural effusion in a previously treated patient, but many nontuberculous causes must be considered as well. Among these are pneumonia, pulmonary emboli, trauma, tumor, pleurodynia, connective tissue disease and others.

Appendix I-E

Procedures for Therapeutic Drug Monitoring of Patients

Therapeutic drug monitoring (TDM) should be done when there is a clear indication for it. Routine monitoring of antituberculosis drug levels is not recommended in clinical practice. The significance of low serum levels of antituberculosis drugs in relation to clinical response has not been demonstrated. Studies have shown that as many as 60% of TB patients had low serum levels of isoniazid or rifampin. However, the clinical response to TB therapy did not differ in those with low drug levels when compared to those with normal levels.

Nonetheless, some patients will fail to respond to antituberculosis treatment despite documented adherence to the medications and absence of drug resistance. Some of these patients may have malabsorption syndromes that prevent them from achieving therapeutic levels of these drugs. Diseases such as HIV infection, cystic fibrosis, diabetes and sprue have been implicated in malabsorption of antituberculosis drugs.

A select number of patients with drug susceptible TB will therefore require drug level testing at some point during their treatment for tuberculosis. Patients with drug-resistant TB are more likely to require drug level testing.

In order to optimize the treatment of patients with TB while maintaining the highest levels of sound medical practice the Bureau of Tuberculosis Control (BTBC) recommends that TDM be used in the following circumstances:

- Lack of clinical response (i.e., culture conversion) while on appropriate drugs and doses, on directly observed therapy (DOT) for at least 2 months and in the absence of drug resistance;
- Lack of clinical response from 2nd-line drugs with a narrow therapeutic window, such as cycloserine, when alternative drugs are limited, and when plans are in place to increase the dose of the drug should levels be low;
- Patients with few effective drugs in their regimen, in order to optimize the effect of available drugs;
- Lack of clinical response (i.e., lack of culture conversion at 2 months) in a patient with known or suspected malabsorption syndrome;
- Patients with renal insufficiency and who have multidrug resistant tuberculosis (MDRTB) or are on certain drugs such as ethambutol;
- Patients who relapse with active TB despite appropriate therapy.

If drugs levels are low and doses are increased, clinical monitoring should be used to judge the response; TDM should only be done when there is no clinical response after a reasonable amount of time.

Patients with pansensitive, cavitary, or otherwise very extensive disease tend to have a delayed clinical response to treatment even when adherence is documented (under DOT). In most cases these patients will respond if given enough time, usually in the third month of therapy. All patients with a delayed response (i.e., lack of culture conversion at 2 months) should be treated for 9 months instead of 6 months.

In order to obtain accurate results BTBC staff must adhere strictly to the guidelines on specimen procurement and handling. Failure to do so will lead to inaccurate results, which may ultimately harm the patient. The following sections delineate procedures for obtaining and handling specimens for TDM.

Physicians

1. Order blood drawing for approximately 2 hours after an observed dose of antituberculosis medications (for para-aminosalicyclic acid [PAS], the blood must be drawn 5 hours after ingestion of PAS granules). Since the serum must be frozen immediately after being centrifuged, do not schedule a blood drawing if the freezer is not functional or not available.

2. For most assays, continue all other antituberculosis medication as usually given. However, if kanamycin is to be assayed, withhold all other antibiotics and antituberculosis medications for 24 hours prior to dosing. After giving kanamycin, draw a 2-hour post dose blood sample. It is no longer necessary to withhold other medications if capreomycin is being monitored. The assay process for this drug has changed. If you are requesting TDM for streptomycin inquire if patient is taking ampicillin and record this on requisition form.

Phlebotomists

1. Draw blood 2 hours after an observed dose of anti-tuberculosis medication(s). One plain 10 ml red-top tube provides enough serum for 2 drugs to be assayed. Serum separator tubes (SST) may be used, but plain red-top tubes are preferred.

2. Approximately 30–60 minutes after drawing blood, centrifuge the specimen until the serum is fully separated and place the specimen in a 2 ml cryovial.

3. After placing the serum in a cryovial, label the cryovial with the patient's name, the center's name, the date and time the blood was drawn, and the name of the drug(s) to be assayed. Complete a National Jewish Medical and Research Center's Infectious Disease Pharmacokinetics Laboratory (IDPL) Requisition Form to accompany the sample. Available at www.njc.org/pdf/Infectious_Disease_Pharm_Lab.pdf

4. Place the cryovial with the label in the freezer compartment in the chest center for a minimum of 8 hours or until the sample is frozen solid, whichever is longer.

5. On the day after blood drawing, when the serum is frozen solid, arrange to have the frozen sample and ice packs picked up and transported directly to the Bureau of Public Health Laboratories (PHL) in a cooler with ice packs. Send a requisition form with the serum sample. Call the Mycobacteriology Laboratory (Room 259) at (212) 447-6745 to alert the laboratory to expect specimens. At PHL the specimen will be inspected and placed immediately in a –70° C refrigerator.

Bureau of Public Health Laboratory

1. At PHL, the sample will be frozen overnight at minus 70° C; the next day it will be packed in dry ice and labeled as specified in full compliance with the shipper and guidelines on handling of dry ice and potentially infectious materials. The requisition form sent with the specimen will be included in the shipping package.

2. PHL staff will call the shipper to pick up and deliver the samples.

3. PHL will alert National Jewish about the arrival of the specimen at 303-398-1974.

4. PHL staff will return ice packs and coolers to the appropriate center. All packs and coolers should be marked with the name and address of the center that sent them.

National Jewish Medical and Research Center

1. Results will be sent from National Jewish to the center directly.

2. National Jewish will bill the BTBC and the bill will go directly to Internal Accounting. Packaging slips and/or any other accompanying slips should be sent to the BTBC Office of Operations.

Appendix I-F

Potential Drug Interactions with Antituberculosis Medications*

Antituberculosis Medication	Drug or Drug Type** (most common brand names)	Potential Interaction
Aminoglycosides		
	ACE inhibitors	↑ Nephrotoxicity
	Antifungal, Amphotericin B (Amphotec®)	↑ Neprotoxicity (synergistic)
	Aminoglutethimide (Cytadren®)	↑ Nephro- and ototoxicity
	Botulinum toxin type A	Possible ↑ effect of the toxin
	Bumetanide (Bumex®)	↑ Ototoxicity (additive)
	Capreomycin (Capastat®)	↑ Oto- and nephrotoxicity (additive)
	Carmustine (BiCNU®)	↑ Nephrotoxicity
	Cephalosporins	↑ Nephrotoxicity
	Chloroquine (Aralen®)	↑ Ototoxicity
	Cisplatin (Platinol®)	↑ Nephrotoxicity
	Colistine Sulfate (Coly-Mycin®)	↑ Nephrotoxicity
	Cyclosporine (Neoral®)	↑ Nephrotoxicity (possible additive or synergistic)
	Deferoxamine (Desferal®)	↑ Nephro- and ototoxicity
	Diuretics	↑ Ototoxicity (synergistic)
	Enflurane (Ethrane®)	Possible nephrotoxicity
	Ethacrynic acid (Edecrin®)	Ototoxicity (additive)
	Furosemide (Lasix®)	↑ Oto- and nephrotoxicity
	Gallium (Ganite®)	Nephrotoxicity (additive)
	Gold salts	Possible ↑ nephrotoxicity
	Hydroxychloroquine (Plaquenil®)	Possible ↑ nephrotoxicity
	Lithium (Lithobid®, Lithotabs®)	↑ Oto- and nephrotoxicity
	Magnesium sulfate	↑ Neuromuscular blockade (additive)
	Malathion (Ovide®)	Possible respiratory depression (additive)
	Methotrexate (Rheumatrex®)	Possible ↑ methotrexate toxicity
	Neostigmine (Prostigmin®)	Decreased effects of neostigmine
	Neuromuscular blocking agents (Pavulon®, Norcuron®)	↑ Neuromuscular blockade (additive)
	Nonsteriodal anti-inflammatory	Acute renal failure with ibuprofen
	Penicillins	↓ Aminoglycoside effect with high concentrations of carbenicillin, ticarcillin, or piperacillin (inactivation)
	Polymyxins (Aerosporin®)	Neprotoxicity, ↑ neuromuscular blockade (additive)
	Vancomycin (Vancocin®)	Possible ↑ oto- and nephrotoxicity (additive)

Antituberculosis Medication	Drug or Drug Type** (most common brand names)	Potential Interaction
Aminoglycosides		
	Vincristine (Oncovin®)	Possible ↑ oto- and nephrotoxicity (additive)
	Zalcitabine (Hivid®)	Possible ↑ risk of peripheral neuropathy (additive)
Cycloserine		
	Alcohol	↑ Alcohol effect or convulsions
	Ethionomide	↑ CNS effect of cycloserine
	Isoniazid (Nydrazid®)	↑ CNS effect, dizziness, drowsiness
Ethionamide		
	Cycloserine (Seromycin®)	↑ CNS effect of cycloserine
	Efavirenz (Sustiva®)	↓ Levels of ethionamide
	Excess ethanol	Possible psychotic reaction
	Isoniazid (Nydrazid®)	↑ Serum concentrations of INH, toxic psychosis and peripheral neuritis (case report)
	Nevaripine (Viramune®)	↓ Levels of ethionamide
	Non-nucleoside reverse transcriptase inhibitors	↑ Levels of ethionamide
	Protease inhibitors	↑ Levels of ethionamide
Fluoroquinolones		
	Amiodarone (Cordarone®)	Possible QT prolongation & arrhythmia with levofloxacin & probably moxifloxacin
	Antacid with metal cations	↓ Fluoroquinolones effect with aluminum, magnesium, or calcium
	Anticoagulants, oral	↑ Anticoagulant effect
	Antifungal, imidazole & triazoles	Possible QT prolongation & torsades de pointes with fluconazole & levofloxacin
	Antidepressants, tricyclic (TCA)	Possible QT prolongation (levofloxacin)
	Arsenic trioxide (Trisenox®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Benzodiazepines (Valium®)	Possible diazepam toxicity with ciprofloxacin
	Bepridil (Vascor®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Beta-adrenergic blockers	Possible metoprolol toxicity with ciprofloxacin, possible QT prolongation with sotalol and moxifloxacin
	Caffeine	Possible caffeine toxicity with ciprofloxacin
	Calcium	↓ Fluoroquinolone effect
	Calcium polycarbophil	↓ Ciprofloxacin effect
	Cisapride (Propulsid®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Clozapine (Clozaril®)	Possible clozapine toxicity with ciprofloxacin
	Corticosteroids	Possible ↑ risk of Achilles tendon disorders
	Cyclosporine (Neoral®)	Possible cyclosporine toxicity with ciprofloxacin

Abbreviation: CNS = central nervous system

* This is not an exhaustive list of drug interactions. Readers should refer to drug information texts and sources and manufacturer package inserts for the latest and complete information. BTBC has a subscription to The Medical Letter's Drug Interaction Program.

** Use of drug names is for informational purposes only and does not imply endorsement by the New York City Department of Health and Mental Hygiene.

Appendix I-F *(continued)*

Potential Drug Interactions with Antituberculosis Medications*

Antituberculosis Medication	Drug or Drug Type** (most common brand names)	Potential Interaction
Fluoroquinolones		
	Didanosine (Videx®)	↓ Fluoroquinolone effect
	Digoxin (Lanoxin®)	Possible digoxin toxicity with gatifloxacin
	Disopyramide (Disopyramide®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Dofetilide (Tikosyn®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Domperidone (Motilium®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Droperidol (Inapsine®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Duloxetine (Cymbalta®)	Possible duloxetine toxicity with ciprofloxacin
	Foscarnet (Foscavir®)	Seizures with ciprofloxacin
	Hypoglycemics, sulfonylurea	Possible ↑ risk of hypoglycemia
	Halofantrine (Halfan®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Haloperidol (Haldol®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Ibutilide	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Iron (Ferosol®)	↓ Fluoroquinolone effect
	Lithium (Lithobid®)	Possible lithium toxicity with levofloxacin
	Macrolide	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Magnesium citrate (Citroma®)	↓ Fluoroquinolone effect
	Methotrexate (Rheumatex®)	Possible methotrexate toxicity with ciprofloxacin
	Mexiletine (Mexitil®)	Possible mexiletine toxicity
	Narcotics: methadone & congeners	Possible methadone toxicity with ciprofloxacin
	Olanzapine (Zyprexa®)	Possible olanzapine toxicity with ciprofloxacin
	Penicillins	Possible ciprofloxacin toxicity with azlocillin
	Pentamidine (Pentam 300®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Pentoxifylline (Trental®)	Headache due to pentoxifylline toxicity with ciprofloxacin
	Phenothiazines (Compazine®, Mellaril®)	Possible QT prolongation with levofloxacin or moxifloxacin and chlorpromazine, mesoridazine or thioridazine (additive)

Antituberculosis Medication	Drug or Drug Type** (most common brand names)	Potential Interaction
Fluoroquinolones		
	Phenytoin (Dilantin®)	Altered phenytoin effect with ciprofloxacin
	Pimozide (Orap®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Pioglitazone (Actos®)	Possible hypoglycemia
	Probenecid (Probalan®)	↑ Serum levels of fluoroquinolones
	Procainamide (Pronestyl®)	Possible procainamide toxicity
	Pyrazinamide	Possible in ↑ adverse effects with levofloxacin and ciprofloxacin
	Quinidine (Quinaglute®)	Possible QT prolongation with levofloxacin or moxifloxacin (additive)
	Ramelton (Rozerem®)	↑ Ramelton toxicity with ciprofloxacin
	Ranolazine (Ranexa®)	↑ Ranolazine effect with ciprofloxacin
	Rasagiline (Azilect®)	↑ Rasagiline toxicity with ciprofloxacin
	Repaglinide (Prandin®)	Possible hypoglycemia
	Ropinirole (Requip®)	↑ Ropinirole effect with ciprofloxacin
	Ropivacaine (Naropin®)	Possible ↑ risk of ropivacaine toxicity with ciprofloxacin
	Sevelamer (Renagel®)	↓ Effects of oral fluoroquinolones
	Sucralfate (Carafate®)	↓ Fluoroquinolone effect
	Theophyllines	↑ Theophylline toxicity with ciprofloxacin, ↑ Toxicity with concurrent cimetidine
	Thyroid hormones	Possible ↓ levothyroxine effect
	Tizadine (Zanaflex®)	↑ Tizadine toxicity
	Ursodiol (Urso®)	↓ Ciprofloxacin effect
	Zinc (Calcet®)	↓ Fluoroquinolone effect
	Ziprasidone (Geodon®)	Prolonged QT interval and possible fatal arrhythmias with moxifloxacin (additive)
Isoniazid		
	Acetaminophen (Tylenol®)	Acetaminophen toxicity (↑toxic metabolites)
	Alfentanil (Alfenta®)	↓ Plasma clearance, ↑ Duration of action of alfentanil
	Alcohol	↑ Incidence of hepatitis, possible decreased isoniazid effect
	Aminosalicylic acid (Paser®)	Hepatotoxicity (↑ toxic metabolites)
	Antacids (Maalox®, Mylanta®)	↓ Isoniazid absorption

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Appendix I-F *(continued)*

Potential Drug Interactions with Antituberculosis Medications*

Antituberculosis Medication	Drug or Drug Type** (most common brand names)	Potential Interaction
Isoniazid		
	Anticoagulants, oral (Coumadin®)	↑ Anticoagulant effect
	Benzodiazepines	Potential ↑ benzodiazepine toxicity
	Carbamazepines (Tegretol®)	↑ Toxicity of both drugs,
	Cycloserine (Seromycin®)	↑ CNS effects, dizziness, drowsiness
	Disulfiram (Antabuse®)	Psychotic episodes, ataxia (avoid concurrent use)
	Enflurane (Ethrane®)	↑ Neprotoxicity (avoid concurrent use)
	Ethionamide	Toxic psychosis, peripheral neuritis
	Haloperidol (Haldol®)	↑ Haloperidol toxicity
	Ketoconazole (Nizoral®)	↓ Ketoconazole effect (isoniazid and rifampin)
	Meperidine (Demerol®)	↑ Meperidine effect
	Mephenytoin (Mesantoin®)	↑ Mephenytoin effect
	Niacin (Niaspan®)	↓ Niacin effect
	Phenytoin (Dilantin®)	↑ Phenytoin effect
	Rifampin (Rifadin®, Rimactane®)	Hepatotoxicity (possibly ↑ toxic metabolites)
	Stavudine (Zerit®)	↑ Risk of peripheral neuropathy
	Theophyllines (Theodur®, Theolair®)	↑ Theophylline toxicity
	Tyramine-rich foods and beverages	Palpitations, tachypnea, sweating, urticaria, headache, vomiting
	Valproate (Depakene®)	↑ Hepatic and CNS toxicity
	Vincristine (Oncovin®)	Neurotoxicity
	Zalcitabine (Hivid®)	↑ Risk of peripheral neuropathy
Linezolid		
	Citalopram (Celexa®)	↑ Risk serotonin syndrome (additive)
	Diphenhydramine (Benadryl®)	Possible ↑ risk delirium
	Duloxetine (Cymbalta®)	Possible ↑ risk serotonin syndrome (additive)
	Fluoxetine (Prozac®)	↑ Risk serotonin syndrome (additive)
	Fluvoxamine (Luvox®)	↑ Risk serotonin syndrome (additive)
	Monoamine Oxidase Inhibitors	Severe hypertension and possible crisis (additive)
	Paroxetine (Paxil®)	Possible ↑ risk serotonin syndrome (additive)
	Rasagiline (Azilect®)	Severe hypertension and possible crisis (additive)
	Sertraline (Zoloft®)	Possible ↑ risk serotonin syndrome (additive)

Antituberculosis Medication	Drug or Drug Type** (most common brand names)	Potential Interaction
Linezolid (continued)		
	Sympathomimetic amines (phenylpropanolamine, pseudoephedrine, dextromethorphan)	Hypertension
	Tyramine-rich foods and beverages	Hypertension due to ↓ metabolism of MAO
	Venlafaxine (Effexor®)	↑ Risk serotonin syndrome (additive)
Para-aminosalicylic acid		
	Digoxin (Lanoxin®)	Possible ↓ digoxin effect
	Probenecid (Probalan®)	Possible aminosalicylic acid toxicity
	Rifampin (Rifadin®, Rimactane®)	↓ Rifampin effect
Pyrazinamide		
	Allopurinol (Zyloprim®)	↑ Pyrazinamide level by inhibiting xanthine oxidase. Failure of allopurinol to ↓ serum uric acid
	Cyclosporine (Neoral®)	↓ Cyclosporine effect, acute myopathy
	Fluoroquinolones	Possible ↑ in adverse effects with levofloxacin
	Isoniazid (Nydrazid®)	↓ Serum isoniazid levels
	Probenecid (Probalan®)	Antagonizes effects of probenecid
	Rifampin (Rifadin®, Rimactane®)	↑ Risk of severe hepatic toxicity and death (additive)
	Sulfinpyrazone (Anturane®)	Antagonizes effects of sulfinpyrazone
Pyridoxine		
	Barbiturates	↓ Barbiturate effect
	Levodopa	↓ Levodopa effect, but not if taking carbidopa
	Phenytoin (Dilantin®)	↓ Phenytoin effect
Rifampin, Rifabutin and Rifapentine		
	Aminosalicylic acid (Paser®)	↓ Rifampin absorption
	Amiodarone (Cordarone®)	↓ Amiodarone effect
	Amprenavir (Agenerase®)	↓ Amprenavir effect (rifampin), possible ↑ Rifabutin toxicity
	Anticoagulants, oral (Coumadin®)	↓ Anticoagulant effect
	Antidepressants, tricyclic (TCA)	↓ TCA effect
	Antifungals (imidazoles, triazoles)	↓ Fluconazole, itraconazole and ketoconazole effect (rifampin), uveitis with fluconazole and itraconazole (rifabutin)
	Antifungals (terbinafine)	↓ Effect terbinafine
	Aprepitant (Emend®)	↓ Aprepitant effect

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Appendix I-F *(continued)*

Potential Drug Interactions with Antituberculosis Medications*

Antituberculosis Medication	Drug or Drug Type** (most common brand names)	Potential Interaction
Rifampin, Rifabutin and Rifapentine		
(continued)	Atazanavir (Reyataz®)	↓ Atazanavir effect, ↑ rifabutin toxicity
	Atovaquone (Malarone®)	↓ Atovaquone effect, ↑ rifampin effect
	Barbiturates	↓ Barbiturate effect
	Benzodiazepines	↓ Benzodiazepine effect that undergo oxidative oxidation such diazepam, alprazolam, midazolam, and triazolam
	Beta-adrenergic blockers	↓ Beta blockade with atenolol, carvedilol, propranolol, or metoprolol (rifampin >> rifabutin)
	Buspirone (BuSpar®)	↓ Buspirone effect
	Carbamazepine (Tegretol®)	↓ Carbamazepine effect
	Caspofungin	↓ Caspofungin effect
	Chloramphenicol (Chloromycetin®)	↓ Chloramphenicol effect
	Chlorpropamide (Diabenese®)	↓ Chlorpropamide effect
	Cimetidine (Tagamet®)	↓ Cimetidine effect
	Citalopram (Celexa®)	↓ Citalopram effect
	Clarithromycin (Biaxin®)	↓ Clarithromycin effect
	Clofazimine (Lamprene®)	Possible ↓ rifampin effect
	Clofibrate (Atromid-S®)	Possible ↓ clofibrate effect
	Clozapine (Clozaril®)	↓ Clozapine effect
	Contraceptives, combination, hormonal	↓ Contraceptive effect (↓ ethinyl estradiol and norethindrone) (rifampin > rifabutin)
	Corticosteroids	Marked ↓ corticosteroid effect
	COX-2 inhibitors (Vioxx®, Celebrex®)	↓ Rofecoxib and celecoxib effect
	Cyclosporine (Neoral®)	↓ Cyclosporine effect
	Dapsone (Dapsone®)	Possible ↓ dapsone effect (rifabutin > rifampin)
	Delavirdine (Resciptor®)	Marked ↓ delavirdine effect (rifampin and rifabutin), ↑ rifabutin effect
	Digitoxin (Crystodigin®)	↓ Digitoxin effect
	Digoxin (Lanoxin®)	↓ Digoxin effect
	Diltiazem (Cardizem®)	↓ Diltiazem effect
	Disopyramide (Norpace®)	↓ Disopyramide effect
	Dolasetron (Anzemet®)	Possible ↓ dolasetron effect

Antituberculosis Medication	Drug or Drug Type** (most common brand names)	Potential Interaction
Rifampin, Rifabutin and Rifapentine (continued)	Domperidone (Motilium®)	Possible ↓ domperidone effect (rifampin and rifabutin)
	Doxycycline (Vibramycin®)	↓ Doxycycline effect
	Efavirenz (Sustiva®)	↓ Efavirenz effect (rifampin), possible ↓ rifabutin effect
	Enalapril (Vasotec®)	↓ Enalapril effect
	Erlotinib (Tarceva®)	Possible ↓ erlotinib effect
	Erythromycin (Ery-Tab®)	↓ Erythromycin effect
	Estrogens	↓ Estrogen effect
	Eszopiclone (Lunesta®)	Possible ↓ eszopiclone effect
	Etravirine (TMC-125)	Possible ↓ etravirine effect (rifampin)
	Fexofenadine (Allegra®)	Possible ↓ fexofenadine effect
	Fluconazole	↓ Fluconazole effect
	Folic Acid	↓ Microbiological assay of serum folate
	Fos-amprenavir (Lexiva®)	↓ Fos-amprenavir effect (rifampin), possible ↑ rifabutin toxicity
	Gefitinib (Iressa®)	↓ Gefitinib effect
	Glimepiride (Amaryl®)	↓ Glimepiride effect
	Glyburide (DiaBeta®, Micronase®)	↓ Glyburide effect
	Haloperidol (Haldol®)	↓ Haloperidol effect
	Halothane	Possible ↑ hepatotoxicity
	HMG-CoA reductase inhibitors (Lipitor®, Lescol®, Zocor®)	↓ Fluvastatin and simvastatin effect possible ↑ hepatotoxicity
	Hydroxychloroquine (Plaquenil®)	↓ Hydroxychloroquine effect
	Hypoglycemics, sulfonylurea	↓ Hypoglycemic effect of glyburide, tolbutamide and possibly glipizide
	Indinavir (Crixivan®)	Marked ↓ indinavir effect (rifampin), possible ↑ Rifabutin toxicity
	Isoniazid (Nydrazid®)	↑ Hepatotoxicity (↑ toxic metabolites)
	Itraconazole (Sporanox®)	↓ Itraconazole effect
	Ketoconazole	↓ Ketoconazole and rifampin effect
	Lamotrigine (Lamictal®)	↓ Lamotrigine effect
	Leflunomide (Arava®)	Possible leflunomide toxicity
	Levothyroxine (Levoxyl®)	↓ Levothyroxine effect

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Appendix I-F *(continued)*

Potential Drug Interactions with Antituberculosis Medications*

Antituberculosis Medication	Drug or Drug Type** (most common brand names)	Potential Interaction
Rifampin, Rifabutin and Rifapentine		
(continued)	Lopinavir/ritonavor (Kaletra®/ Norvir®)	↓ Lopinavir/ritonavir effect (rifampin), possible ↑ rifabutin toxicity
	Losartan (Cosaar®)	Possible ↓ losartan effect
	Macrolide antibiotics	↓ Macrolide effect, ↑ rifabutin toxicity (clarithromycin)
	Maraviroc (Selzentry®)	↓ Maraviroc effect (rifampin)
	Mefloquine (Lariam®)	↓ Mefloquine effect
	Mephenytoin (Mesantoin)	↓ Mephenytoin effect (rifampin)
	Metoprolol	Possible ↓ beta blockade
	Metronidazole (Flagyl®)	↓ Metronidazole effect
	Mexiletine (Mexitil®)	↓ Antiarrhythmic effect
	Morphine (Avinza®)	↓ Morphine effect
	Moxifloxacin (Avelox®)	↓ Moxifloxacin effect (with intermittently dosed rifampin)
	Narcotics/opiates	Cross-reactivity & false positive urine screening tests
	Narcotics: Methadone, Congeners	↓ Methadone effect (rifampin, rifabutin) withdrawal symptoms
	Narcotics: Morphine-like	Possible ↓ codeine or morphine response
	Nateglinide (Starlix®)	↓ Nateglinide effect
	Nelfinavir (Viracept®)	Marked ↓ nelfinavir effect, possible ↑ rifabutin toxicity
	Nevirapine (Viramune®)	↓ Nevirapine effect (rifampin) possible ↑ Rifabutin toxicity
	Nifedipine (Adalat®)	↓ Antihypertensive effect
	Nisoldipine (Sular®)	↓ Antihypertensive effect
	Ondansetron (Zofran®)	↓ Ondansetron effect
	Phenytoin (Dilantin®)	↓ Phenytoin effect
	Pioglitazone (Actos®)	Possible ↓ pioglitazone effect
	Pravastatin (Pravachol®)	Possible ↓ pravastatin effect
	Praziquantel (Biltricide®)	↓ Praziquantel effect
	Probenecid (Probalan®)	Possible ↑ rifampin effect
	Progestin	↓ Progestin (norethindrone) effect
	Propafenone (Rythmol®)	↓ Propafenone effect

Antituberculosis Medication	Drug or Drug Type** (most common brand names)	Potential Interaction
Rifampin, Rifabutin and Rifapentine (continued)	Pyrazinamide	Possible ↑ hepatotoxicity and death (additive)
	Quetiapine (Seroquel®)	↓ Quetiapine effect
	Quinidine (Quinaglute®)	↓ Quinidine effect
	Quinine (Quindan®)	↓ Quinine effect
	Radiocontrast media	↓ Biliary excretion of contrast media
	Raltegravir (Isentress™, MK0518)	Possible ↓ raltegravir effect (rifampin)
	Ramelteon (Rozerem®)	Possible ↓ ramelteon effect
	Ranolazine (Ranexa®)	↓ Ranolazine effect
	Repaglinide (Prandin®)	Possible ↓ repaglinide effect
	Ritonavir	Possible ↓ ritonavir effect (rifampin), ↑ Rifabutin toxicity
	Ropivacaine (Naropin®)	Possible ↓ ropivacaine effect
	Rosiglitazone (Avandia®)	↓ Rosiglitazone effect
	Saquinavir (Fortovase®)	↓ Saquinavir effect (rifampin rifabutin) Possible ↑ rifabutin toxicity
	Sertraline (Zoloft®)	↓ Sertraline effect
	Sirolimus (Rapamune®)	↓ Sirolimus effect
	Sulfonamides	Possible ↓ sulfamethoxazole effect (rifampin), ↑ Risk sulfamethoxazole toxicity (rifabutin)
	Tacrolimus (Prograf®)	↓ Tacrolimus effect
	Tadalafil (Cialis®)	↓ Tadalafil effect
	Tamoxifen (Nolvadex®)	Possible ↓ tamoxifen effect
	Telithromycin (Ketex®)	Possible ↓ telethromycin effect Possible ↑ hepatotoxicity
	Tetracyclines (Sumicin®)	↓ Tetracycline effect
	Theophyllines (Uni-Dur®)	↓ Theophylline effect
	Thyroid hormones	↓ Thyroid hormone effect
	Tinidazole (Tindamax®)	Possible ↓ tinidazole effect (rifampin)
	Tocainide (Tonocard®)	Possible ↑ tocainide effect
	Toremifene (Fareston®)	Possible ↓ toremifene effect
	Trazadone	Possible ↓ trazadone effect
	Trimethoprim	↓ Trimethoprim effect

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Appendix I-F *(continued)*

Potential Drug Interactions with Antituberculosis Medications*

Antituberculosis Medication	Drug or Drug Type** (most common brand names)	Potential Interaction
Rifampin, Rifabutin and Rifapentine (continued)	Trimethoprim-sulfamethoxazole (Bactrim®)	Possible ↑ rifampin toxicity, possible ↓ Trimethoprim-sulfamethoxazole effect (rifampin and rifabutin)
	Sulfobromophthalein	↓ Hepatic uptake of sulfobromophthalein sodium
	Verapamil (Isoptin®)	↓ Verapamil effect
	Vitamin B_{12}	Inhibits microbiological assays for vitamin B_{12}
	Voriconazole (Vfend®)	↓ Voriconazole effect, possible ↑ rifabutin toxicity
	Zaleplon (Sonata®)	↓ Zaleplon effect
	Zidovudine (Retrovir®, AZT)	Possible ↓ zidovudine effect
	Zolpidem (Ambien®)	↓ Zolpidem effect

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Appendix I-G

The Use of Bacille Calmette-Guérin Vaccine

Bacille Calmette-Guérin (BCG) vaccine[1] is a live, attenuated strain of *Mycobacterium bovis*. In most parts of the world, BCG vaccine is used routinely to prevent serious complications of TB, such as miliary TB and central nervous system (CNS) TB, in infants and children and in health care workers with frequent exposure to individuals with infectious TB.

Although the evidence is conflicting, a large body of research indicates that BCG vaccination does not completely prevent latent TB infection (LTBI) or pulmonary TB. Some studies suggest that BCG vaccination lessens the likelihood of disseminated TB and TB meningitis, especially in infants.

In the United States, BCG vaccine is not recommended routinely for children or used as a control strategy against TB. Specifically, it is not recommended as a general preventive strategy for health care workers because it complicates the interpretation of tuberculin skin test (TST) reactions and because it has not been proven effective in preventing LTBI. Health care workers who work primarily with patients who have multidrug-resistant TB (MDRTB) should be counseled on the risks and benefits of BCG vaccine.

BCG is not recommended for HIV-infected children or adults, and HIV testing must be performed before BCG is administered. Similarly, active TB must be ruled out before BCG can be given.

Nonetheless, BCG vaccine may be considered in very specific circumstances. These circumstances include instances in which infants and children are close household contacts of an individual with persistently untreated or ineffectively treated smear-positive TB, especially MDRTB.

On occasion, it may make clinical sense to give BCG to a young child who is going to live in a TB-endemic area for a prolonged period.

As of February 2007, Organon Pharmaceuticals (800) 631-1253 has vaccine available through a wholesale distributor. In addition, the TICE BCG vaccine is available from the manufacturer IVES.

All requests for BCG must be approved by the Director, Bureau of Tuberculosis Control, or a designee. BCG vaccine can be obtained from the principal pharmacist, STD/TB Pharmacy, New York City Department of Health and Mental Hygiene, 455 First Avenue, Room 147, NY, NY 10016. Telephone: (212) 447-2209.

1. Indications and Contraindications for Bacille Calmette-Guérin Vaccine

Before deciding to give BCG vaccine to a contact of an individual with persistently untreated or ineffectively treated smear-positive TB, every effort should be made to (1) ensure that the inadequately treated individual with infectious TB is treated properly, and to (2) separate the individual with TB and the exposed contact(s).

If this is not possible, giving BCG vaccine may be considered if the contact meets **all** of the following criteria:

- The contact has a negative test for TB infection (TTBI).
- The contact is repeatedly exposed to an individual with persistently untreated or ineffectively treated smear-positive MDRTB (TB resistant to isoniazid and rifampin).
- The contact is HIV-negative. (In some situations, however, BCG vaccine may be given to infants who have a positive HIV antibody as below.)

Notes:

1. Product names are provided for identification purposes only; their use does not imply endorsement by the New York City Department of Health and Mental Hygiene.

BCG vaccine should not be given to the following individuals:

- Persons with a documented history of a positive reaction to a TTBI
- Persons who are HIV-positive or otherwise immunosuppressed
- Persons with behavioral risk factors for HIV infection who decline HIV testing

There have been no reports of harmful effects of BCG vaccine on the fetus. Nevertheless, giving BCG vaccine should be avoided in pregnant women, unless there is an unusual risk of unavoidable exposure to infectious MDRTB.

2. Special Considerations for Infants

At least 2 other factors must be weighed before a decision is made to give BCG vaccination to a newborn or infant younger than 9 months old:

- Because an infant may not be able to mount a cellular immune response to infection with *M. tb*, a TST may not be a reliable indicator of infection. Thus, there may be instances where an infant with a negative TST may receive BCG vaccine even though he or she may be infected with *M. tb*.
- The blood of some infants born to mothers who are HIV infected may show the presence of placentally transferred HIV antibodies for a number of months after birth, even if the infant is not infected with HIV. Because HIV infection cannot be excluded in this situation, BCG vaccine could be considered if the infant is otherwise healthy, especially if the evaluation of other close contacts reveals a high rate of documented TST conversions and if all other efforts to prevent transmission have failed. Such an infant needs to be followed by a specialist until HIV infection is ruled out based on the most current recommendations.

3. Evaluation and Follow-up

- An individual who is being considered for BCG vaccination who cannot document a history of a previous positive TST reaction should have a TST, using 5 tuberculin units of purified protein derivative (PPD). A blood based test is not recommended in this setting.
- An individual who is being considered for BCG vaccination should be offered HIV counseling and testing if he or she has risk factor(s) for HIV infection.
- If the individual being considered for BCG vaccination is an infant or child, the parent or legal guardian must be interviewed and must agree. This must be documented in the chart.
- Eight weeks after the administration of BCG vaccine, the individual should have a repeat TST performed to document any reaction. If the contact's TST is < 5 mm, the BCG vaccination should be repeated.
- There is no evidence that revaccination with BCG affords any additional protection and therefore revaccination is not recommended.

4. New Blood-based Test for Tuberculosis Infection

- The new blood-based tests will differentiate between infection with BCG and *M. tb*. In this case, a blood-based test may be a reliable indicator of TB infection as the test can differentiate between *M. tb*. complex and most other atypical mycobacteria.

Appendix II-A

Reporting Requirements for Suspected or Confirmed Tuberculosis

Medical providers and infection control practitioners are required by the New York City Health Code Article 11, in particular, Sections 11.03, 11.05 and 11.47(a), to report all patients suspected and confirmed with tuberculosis (TB) to the New York City Department of Health and Mental Hygiene (DOHMH), Bureau of Tuberculosis Control (BTBC) within 24 hours of the time the diagnosis is first suspected. Medical providers must report these patients even though microbiologists and pathologists are also required to report findings consistent with TB. Note that the reports have to be received by the DOHMH within 24 hours, whether by express or overnight mail, fax, telephone or electronically.

It is **mandatory** to report patients who meet ***any*** of the following criteria:

- Smear (from any anatomic site) positive for acid-fast bacilli (AFB)
- Rapid diagnostic tests, such as nucleic acid amplification test (NAA) (e.g., Roche's AMPLICOR®, Genprobe's MTD™)[1] result suggests *Mycobacterium tuberculosis (M. tb.) complex*
- Culture positive for *M. tb complex* including: *M. tb.*, *M. africanum*, *M. bovis-BCG*, *M. caprae*, *M. canettii*, *M. microti*, *M. pinnipedii*, *M. bovis*
- Biopsy, pathology or autopsy findings consistent with active tuberculosis disease, including but not limited to caseating granulomas in biopsy of lung, lymph nodes or other specimen
- Treatment with 2 or more anti-TB medications for suspected or confirmed active TB
- Clinical suspicion of pulmonary or extrapulmonary tuberculosis such that the physician or other health care provider has initiated or intends to initiate isolation or treatment for TB
- Continuation, discontinuation, completion, or other outcomes of treatment for TB
- Contact of an active TB case receiving treatment for TB infection
- Any child younger than five years old (up to the day of the fifth birthday) who has a positive result on a tuberculin skin test or a positive U.S. Food and Drug Administration (FDA) approved blood-based test for TB infection (such as Quantiferon)[2]
- In addition, Section 47.21 requires that Day Care staff report those with LTBI to the Bureau of Day Care

When an individual has an AFB-positive smear or has started treatment for TB, reporting should never be delayed pending identification of *M. tb.* with rapid diagnostic tests (e.g., NAA tests). Patients should be reported whenever TB is suspected, even if bacteriologic evidence of disease is lacking or treatment has not been initiated.

Microbiology and Pathology Laboratories

The New York City Health Code also requires laboratories to report as per Articles 11 and 13, Sections 11.03, 11.05 and 13.03, all of the following to the New York City DOHMH, BTBC:

- AFB-positive smears (regardless of anatomic site)
- Cultures positive for *M. tb*. complex
- Any culture or NAA result associated with an AFB-positive smear (even if negative for *M. tb*. complex)
- Rapid diagnostic test results that identify *M. tb*. complex (e.g., AMPLICOR®, MTD™)
- Results of susceptibility tests performed on *M. tb*. complex cultures
- Pathology findings consistent with TB, including the presence of AFB and granulomas

Reporting by Telephone and on the Universal Reporting Form

All suspected and confirmed TB patients may be reported by telephone to the TB Hotline, (212) 788-4162, but a completed Universal Reporting Form (URF) must follow within 48 hours.[2] The URF should be faxed to the BTBC at (212) 788-4179 and the original mailed to DOHMH at 125 Worth Street, Room 315, CN-6 NY, NY 10013. The URF can also be completed online, by first creating an account on NYC-MED at www.nyc.gov/health/nycmed. Assistance is available by calling (888) NYC-MED9 or (212) 442-3384.

Information reported on the URF should be as complete as possible. The following essential information must be included when the report is submitted to the New York City DOHMH:

- Information needed to identify and locate the individual (i.e., name, telephone number, address, and date of birth)
- Provider information (i.e., physician's name and telephone number, reporting facility)
- Results of smear for AFB (including the date the specimen was obtained and the accession number, if available)
- Results of chest radiographs

Laboratories can report via the Electronic Clinical Laboratory Reporting System (ECLRS). As of July 1, 2006, ECLRS will be the mandatory method of laboratory reporting in New York City. Assistance with ECLRS is available by calling (212) 442-3380. In addition, within 24 hours of observing growth of *M. tb.* complex in a culture from any specimen, the New York City Health Code Section 13.05(a) requires that a portion of the initial culture be sent to the NYC DOHMH Public Health Laboratory, 455 First Avenue, Room 236, New York, NY 10016, for DNA analysis,. Laboratories outside of New York City will submit isolates directly to the New York State Wadsworth Center Mycobacteriology Laboratory in Albany, NY for genotyping.

Patient Follow-up

Treating physicians should also report whether the patient completed treatment and the outcome of the patient (cured, failed, relapsed, lost, moved) or whether treatment was discontinued if the patient was found not to have TB. Physicians must assist the DOHMH in its efforts to evaluate persons suspected of having TB and in patient follow-up. Case managers will be in contact with the treating physicians to request updates and ensure that appropriate treatment and monitoring is being conducted. A Report of Patient Services Form (TB 65) may need to be completed.

Reporting Tuberculosis-Related Evaluation and Treatment of Contacts

Medical providers are required, under Section 11.47(b) of the New York City Health Code, to report to the DOHMH, when requested, all informatioin on the evaluation, testing, and treatment of individuals who have been in contact with a person with active TB disease.

Inquiries and Forms

To inquire further about reporting procedures, please call the BTBC Surveillance Office at (212) 788-4162. To order copies of the Report of Patients Services Form (TB 65) call (212) 442-5100. Obtain the URF by calling toll free (866) NYC-DOH1 (866 692-3641) or at www.nyc.gov/html/hcp/hcp-urf2.shtml.

Notes:

2. For guidelines for interpreting skin test results, see City Health Information: Testing and Treating for Latent TB Infection, April 2006, www.nyc.gov/html/doh/downloads/pdf.chi.chi25-4.pdf.

Appendix II-B

Procedures for Follow-Up of Centers for Disease Control Tuberculosis-Classified Immigrants and Refugees by the Bureau of Tuberculosis Control/Immigration and Refugee Unit

A medical examination that includes chest X-ray (CXR) for tuberculosis (TB) evaluation is mandatory for all refugees coming to the U.S. and all applicants outside the U.S. applying for an immigrant visa, and those who are applying for immigration status while already in the U.S., in accordance with the Immigration and Nationality Act and the Public Health Service Act.

Outside the U.S., medical examinations are performed by panel physicians selected by the Department of State (DOS) consular officials. The Division of Global Migration and Quarantine (DGMQ) at the Centers for Disease Control and Prevention (CDC) provide the DOS and the U.S. Citizenship and Immigration Services (USCIS) with medical screening guidelines for all examining physicians, which outline in detail the scope of the medical examination. DGMQ also provides the Technical Instructions for Medical Examination of Aliens (TI) and guidance to panel physicians conducting the medical examination including the CXR and any necessary laboratory procedures for tuberculosis evaluation for migration. (The TI is currently under revision.) The panel physicians are required to complete Medical Examination for Immigrant and Refugee Form DS-2053 and the CXR and Classification Worksheet Form DS-3024, DS-3026 with a classification of the patient into one of the following categories:

Class A: Non-Communicable for Travel Purposes

- Abnormal chest radiograph(s) suggestive of current pulmonary TB
- History of one or more sputum smear exams positive for acid-fast bacilli
- Currently on recommended TB treatment **AND**
- Sputum smears negative for AFB on 3 consecutive days while on treatment

A waiver is required for such applicants to travel to the U.S.

Class B1: Tuberculosis Pulmonary, Clinically Active, Noninfectious

- Abnormal chest X-ray (CXR) suggestive of current pulmonary TB
- Sputum smears negative for AFB on 3 consecutive days

Class B1: Tuberculosis Extrapulmonary, Clinically Active, Noninfectious

- Radiographic or other evidence of extrapulmonary TB

Class B2: Tuberculosis, Inactive, Noninfectious

All immigrants and refugees with a CDC TB classification are given the CXR films along with DS-forms (overseas medical evaluation forms) to bring to the United States. The medical evaluation forms are collected at the U.S. ports of entry by the Homeland Security Inspectors and passed on to the local CDC DGMQ office. The overseas CXR films are not collected at the ports of entry. The regional DGMQ offices issue a letter from the CDC to migrants indicating their tuberculosis status asking them to contact the Health Department in their resettlement jurisdiction.

The regional DGMQ offices transmit all DS-forms and other overseas medical documents collected from immigrants and refugees at the U.S. ports of entry to the CDC-DGMQ central office in Atlanta via Electronic Disease Notification (EDN), a CDC initiated web-based notification system via Secure Data Network (SDN). The DGMQ central office inputs all alien data, DS-forms and medical documents into EDN, and generates a Follow-Up Worksheet for TB classified aliens and transmits them to designated health jurisdictions via EDN. The DGMQ then sends email notifications to receiving jurisdictional EDN

TB coordinators. The DGMQ transmits notifications to NYC BTBC/IRU of TB classified aliens who have indicated New York City as their destination in the U.S.

Bureau of Tuberculosis Control/Immigration and Refugee Unit Procedures

Upon receipt of CDC email notifications, the BTBC/IRU accesses EDN to view, download and print all alien documents and TB Follow-up Worksheets entered in EDN and processes domestic evaluation and follow-up of all notified aliens.

The IRU public health advisers (PHAs) immediately contact above notified immigrants and refugees, interview them and collect their overseas CXR films. The IRU case managers create individual charts for each TB classified alien consisting of all documents downloaded and printed from the EDN system, overseas CXR, IRU Evaluation form and BTBC Universal Referral Form. The charts are given to the BTBC assigned medical consultant for re-reading of CXR and review of medical examination documents. The medical consultant records his reading of chest radiographs and documents instructions for necessary follow-up as follows:

1. Refer immediately to chest center/clinic-highly suspicious of TB;
2. Refer to chest clinic-rule out TB:
3. Refer for TTBI-normal CXR;
4. Non-TB condition-referral to medical clinic recommended;
5. No follow-up-no follow-up necessary;

In general, the CXR abnormalities can be grouped as follows:

1. Changes that suggest active TB, such as cavities, "soft" infiltrates, etc. (Class V [High]). These individuals are promptly notified of their clinical situation, and an appointment is made as soon as possible at a nearby New York City Bureau of Tuberculosis Control (BTBC) chest center. The BTBC/IRU follows subsequent events to ensure that these individuals keep their appointment and receive an evaluation. This group accounts for about 5% of all individuals with an abnormal CXR.
2. Changes that suggest inactive TB, such as non-calcified nodules, linear densities, etc., but thought to be sufficient to warrant treatment for active tuberculosis or latent TB infection (LTBI) (Class V [Low]). These individuals are also given appointments in a chest center for medical evaluation and treatment. This group accounts for about 40% of all individuals with an abnormal CXR.
3. Changes that were reported as abnormal but on review have an indication for treatment of LTBI. Among these are calcified Ghon complex, calcified granuloma, apical "caps," pleural thickening, bullae, etc. Individuals with this type of CXR are given an appointment in the BTBC/IRU for a tuberculin skin test (TST). Those with a positive result are referred to a chest center to be evaluated for treatment of LTBI (Class II). This group represents approximately 55% of those with an abnormal CXR.
4. Changes that suggest serious nontuberculous disease include primary or metastatic lung tumor, bronchial obstruction, mediastinal masses, aortic aneurysm, etc. These individuals are contacted and assisted in arranging appointments with a general chest or medical center for appropriate diagnostic investigation and treatment as indicated. These individuals represent 1%-2% of the total.
5. If CXR findings are either normal or findings require no medical follow-up, the alien is notified of such.

The aliens are referred as per medical consultant's recommendations to DOHMH chest centers and non-DOHMH providers for appropriate follow-up and treatment. The IRU case managers contact the referral facilities, obtain clinic appointments for the migrants and notify them of their appointments via phone calls and letters. The PHAs also send referral packages consisting of IRU-created charts to the chest centers/clinics before the scheduled appointment.

In addition, some aliens are referred to DOHMH chest centers for CXRs because they report to have lost their overseas chest radiograph or did not bring it with them from overseas. Some aliens walk in to DOHMH and non-DOHMH chest centers/clinics on their own without any referral from IRU.

The examining physician has to complete the CDC-TB Follow-up Worksheets with diagnostic, follow-up, treatment and outcome data and return them to IRU. The IRU PHAs visit DOHMH chest centers and non-DOHMH facilities and work closely with them to obtain all follow-up data and update the IRU database. IRU users complete Follow-up Worksheets and transmit them to CDC-DGMQ via EDN.

Appendix II-C

Surveillance for Tuberculosis by Health Systems Examination

In New York City, applicants for disability or welfare assistance must have a health examination that is provided by Health Systems Inc., a medical group under contract with New York City. Individuals judged to have a greater-than-average risk of tuberculosis (TB) also receive a chest X-ray (CXR). These include persons with symptoms suggestive of chronic respiratory disease, present or past history of TB, a positive tuberculin skin test or other conditions that increase TB risk. The CXRs are read by a certified radiologist at Health Systems.

CXRs with abnormalities possibly related to TB are referred to the New York City Bureau of Tuberculosis Control (BTBC) for a review and assessment of the need for follow-up. Needed follow-up is provided by the Immigrant and Refugee Health Unit (IRU), organized to conduct this type of surveillance. The CXRs reviewed in the IRU show a variety of abnormalities, ranging from far-advanced cavitary lesions typical of TB (Class V [High]) to those with linear densities or non-calcified nodules, typical of inactive TB (Class V [Low]).

In every case, the next step is a computer search of the TB Registry. Most, but not all, of those with advanced active disease are being treated in a center in New York City. If the registry shows an acceptable level of compliance, no further follow-up is requested. If there is no evidence of TB diagnosis or treatment, or if the patient has been receiving therapy but is delinquent, the IRU locates the individual and attempts to refer the patient to a center for reevaluation and treatment if indicated. At least 27 new cases of culture-positive TB have been identified since this program began in July 1996.

Some individuals have evidence of old, healed TB on the CXR (Class V [Low] or Class IV). If the registry indicates prior therapy and discharge at completion of treatment, no further follow-up is requested in most cases. Otherwise, the individual is referred to a BTBC chest center to be evaluated for treatment of latent TB infection.

A few CXRs show abnormalities consistent with nontuberculous disease, such as bronchial obstruction, mediastinal mass, pleural effusion or other conditions that suggest the need for invasive diagnostic procedures. In this situation, the individual is referred by the IRU to a general chest or medical clinic for appropriate diagnostic investigation and treatment.

Appendix III-A and Appendix III-B

In 2006, the *"International Standards for Tuberculosis Care"** were published to describe a widely accepted level of care that all practitioners, public and private, should seek to achieve in managing patients who have, or are suspected of having, tuberculosis. The same group has also developed the *"Patients' Charter for Tuberculosis Care."* The two documents were developed in tandem and serve as a companion to and support each other.

Appendix III-A International Standards for Tuberculosis Care

The *Standards* are intended to facilitate the effective engagement of all care providers in delivering high-quality care for patients of all ages, including those with sputum smear positive, sputum smear negative, and extra-pulmonary tuberculosis, tuberculosis cause by drug-resistant *Mycobacterium tuberculosis* complex *(M. tuberculosis)* organisms, and tuberculosis combined with human immunodeficiency virus (HIV) infection.

These *Standards* are reproduced here from the above document to serve as a reference for all TB care providers. BTBC guidelines generally adhere to all these *Standards;* however there are some differences but usually BTBC guidelines are more stringent.

Standards for Diagnosis

Standard 1. All persons with otherwise unexplained productive cough lasting two–three weeks or more should be evaluated for tuberculosis.

Standard 2. All patients (adults, adolescents, and children who are capable of producing sputum) suspected of having pulmonary tuberculosis should have at least two, and preferably three, sputum specimens obtained for microscopic examination. When possible, at least one early morning specimen should be obtained.

Standard 3. For all patients (adults, adolescents, and children) suspected of having extrapulmonary tuberculosis, appropriate specimens from the suspected sites of involvement should be obtained for microscopy and, where facilities and resources are available, for culture and histopathological examination.

Standard 4. All persons with chest radiographic findings suggestive of tuberculosis should have sputum specimens submitted for microbiological examination.

Standard 5. The diagnosis of sputum smear-negative pulmonary tuberculosis should be based on the following criteria: at least three negative sputum smears (including at least one early morning specimen); chest radiography findings consistent with tuberculosis; and lack of response to a trial of broad spectrum antimicrobial agents. (NOTE: Because the fluoroquinolones are active against *M. tuberculosis* complex and, thus, may cause transient improvement in persons with tuberculosis, they should be avoided.) For such patients, if facilities for culture are available, sputum cultures should be obtained. In persons with known or suspected HIV infection, the diagnostic evaluation should be expedited.

Standard 6. The diagnosis of intrathoracic (i.e., pulmonary, pleural, and mediastinal or hilar lymph node) tuberculosis in symptomatic children with negative sputum smears should be based on the finding of chest radiographic abnormalities consistent with tuberculosis and either a history of exposure to an infectious case or evidence of tuberculosis infection (positive tuberculin skin test or interferon gamma release assay). For such patients, if facilities for culture are available, sputum specimens should be obtained (by expectoration, gastric washings, or induced sputum) for culture.

* From "Tuberculosis Coalition for Technical Assistance. *International Standards for Tuberculosis Care (ISTC).* The Hague: Tuberculosis Coalition for Technical Assistance, 2006."

Standards for Treatment

Standard 7. Any practitioner treating a patient for tuberculosis is assuming an important public health responsibility. To fulfill this responsibility the practitioner must not only prescribe an appropriate regimen but, also, be capable of assessing the adherence of the patient to the regimen and addressing poor adherence when it occurs. By so doing, the provider will be able to ensure adherence to the regimen until treatment is completed.

Standard 8. All patients (including those with HIV infection) who have not been treated previously should receive an internationally accepted first-line treatment regimen using drugs of known bioavailability. The initial phase should consist of two months of isoniazid, rifampicin, pyrazinamide, and ethambutol. The preferred continuation phase consists of isoniazid and rifampicin given for four months. Isoniazid and ethambutol given for six months is an alternative continuation phase regimen that may be used when adherence cannot be assessed, but it is associated with a higher rate of failure and relapse, especially in patients with HIV infection.

The doses of antituberculosis drugs used should conform to international recommendations. Fixed-dose combinations of two (isoniazid and rifampicin), three (isoniazid, rifampicin, and pyrazinamide), and four (isoniazid, rifampicin, pyrazinamide, and ethambutol) drugs are highly recommended, especially when medication ingestion is not observed.

Standard 9. To foster and assess adherence, a patient-centered approach to administration of drug treatment, based on the patient's needs and mutual respect between the patient and the provider, should be developed for all patients. Supervision and support should be gender-sensitive and age-specific and should draw on the full range of recommended interventions and available support services, including patient counseling and education. A central element of the patient-centered strategy is the use of measures to assess and promote adherence to the treatment regimen and to address poor adherence when it occurs. These measures should be tailored to the individual patient's circumstances and be mutually acceptable to the patient and the provider. Such measures may include direct observation of medication ingestion (directly observed therapy—DOT) by a treatment supporter who is acceptable and accountable to the patient and to the health system.

Standard 10. All patients should be monitored for response to therapy, best judged in patients with pulmonary tuberculosis by follow-up sputum microscopy (two specimens) at least at the time of completion of the initial phase of treatment (two months), at five months, and at the end of treatment. Patients who have positive smears during the fifth month of treatment should be considered as treatment failures and have therapy modified appropriately. (See Standards 14 and 15.) In patients with extrapulmonary tuberculosis and in children, the response to treatment is best assessed clinically. Follow-up radiographic examinations are usually unnecessary and may be misleading.

Standard 11. A written record of all medications given, bacteriologic response, and adverse reactions should be maintained for all patients.

Standard 12. In areas with a high prevalence of HIV infection in the general population and where tuberculosis and HIV infection are likely to co-exist, HIV counseling and testing is indicated for all tuberculosis patients as part of their routine management. In areas with lower prevalence rates of HIV, HIV counseling and testing is indicated for tuberculosis patients with symptoms and/or signs of HIV-related conditions and in tuberculosis patients having a history suggestive of high risk of HIV exposure.

Standard 13. All patients with tuberculosis and HIV infection should be evaluated to determine if antiretroviral therapy is indicated during the course of treatment for tuberculosis. Appropriate arrangements for access to antiretroviral drugs should be made for patients who meet indications for treatment. Given the complexity of co-administration of antituberculosis treatment and antiretroviral therapy, consultation with a physician who is expert in this area is recommended before initiation of concurrent treatment for tuberculosis and HIV infection, regardless of which disease appeared first. However, initiation of treatment for tuberculosis should not be delayed. Patients with tuberculosis and HIV infection should also receive cotrimoxazole as prophylaxis for other infections.

Standard 14. An assessment of the likelihood of drug resistance, based on history of prior treatment, exposure to a possible source case having drug-resistant organisms, and the community prevalence of drug resistance, should be obtained for all patients. Patients who fail treatment and chronic cases should always be assessed for possible drug resistance. For patients in whom drug resistance is considered to be likely, culture and drug susceptibility testing for isoniazid, rifampicin, and ethambutol should be performed promptly.

Standard 15. Patients with tuberculosis caused by drug-resistant (especially multiple drug resistant [MDR]) organisms should be treated with specialized regimens containing second-line antituberculosis drugs. At least four drugs to which the organisms are known or presumed to be susceptible should be used, and treatment should be given for at least 18 months. Patient centered measures are required to ensure adherence. Consultation with a provider experienced in treatment of patients with MDR tuberculosis should be obtained.

Standards for Public Health Responsibilities

Standard 16. All providers of care for patients with tuberculosis should ensure that persons (especially children under 5 years of age and persons with HIV infection) who are in close contact with patients who have infectious tuberculosis are evaluated and managed in line with international recommendations. Children under 5 years of age and persons with HIV infection who have been in contact with an infectious case should be evaluated for both latent infection with *M. tuberculosis* and for active tuberculosis.

Standard 17. All providers must report both new and retreatment tuberculosis cases and their treatment outcomes to local public health authorities, in conformance with applicable legal requirements and policies.

Appendix III-B Patients' Charter for Tuberculosis Care

The *Charter* specifies patients' rights and responsibilities and is meant to serve as a set of standards from the point of view of the patient, defining what the patient should expect from the provider and what the provider should expect from the patient. These standards are meant to empower patients to evaluate the quality of care they are being provided. Good care for individuals with tuberculosis is also in the best interest of the community. These are being reproduced in full in this manual to serve as reference. (See p. 238.)

The Patients' Charter for Tuberculosis Care

Patients' Rights

Patients have the right to:

Care

- The right to free and equitable access to tuberculosis care, from diagnosis through treatment completion, regardless of resources, race, gender, age, language, legal status, religious beliefs, sexual orientation, culture, or having another illness
- The right to receive medical advice and treatment which fully meets the new *International Standards for Tuberculosis Care*, centering on patient needs, including those with multidrug-resistant tuberculosis (MDR-TB) or tuberculosis-human immunodeficiency virus (HIV) coinfections and preventative treatment for young children and others considered to be at high risk
- The right to benefit from proactive health sector community outreach, education, and prevention campaigns as part of comprehensive care programs

Dignity

- The right to be treated with respect and dignity, including the delivery of services without stigma, prejudice, or discrimination by health providers and authorities
- The right to quality healthcare in a dignified environment, with moral support from family, friends, and the community

Information

- The right to information about what healthcare services are available for tuberculosis and what responsibilities, engagements, and direct or indirect costs are involved
- The right to receive a timely, concise, and clear description of the medical condition, with diagnosis, prognosis (an opinion as to the likely future course of the illness), and treatment proposed, with communication of common risks and appropriate alternatives
- The right to know the names and dosages of any medication or intervention to be prescribed, its normal actions and potential side-effects, and its possible impact on other conditions or treatments
- The right of access to medical information which relates to the patient's condition and treatment and to a copy of the medical record if requested by the patient or a person authorized by the patient
- The right to meet, share experiences with peers and other patients, and to voluntary counseling at any time from diagnosis through treatment completion

Choice

- The right to a second medical opinion, with access to previous medical records
- The right to accept or refuse surgical interventions if chemotherapy is possible and to be informed of the likely medical and statutory consequences within the context of a communicable disease
- The right to choose whether or not to take part in research programs without compromising care

Confidence

- The right to have personal privacy, dignity, religious beliefs and culture respected
- The right to have information relating to the medical condition kept confidential and released to other authorities contingent upon the patient's consent

Justice

- The right to make a complaint through channels provided for this purpose by the health authority and to have any complaint dealt with promptly and fairly
- The right to appeal to a higher authority if the above is not respected and to be informed in writing of the outcome

Organization

- The right to join, or to establish, organizations of people with or affected by tuberculosis and to seek support for the development of these clubs and community-based associations through the health providers, authorities, and civil society
- The right to participate as "stakeholders" in the development, implementation, monitoring, and evaluation of tuberculosis policies and programs with local, national, and international health authorities

Security

- The right to job security after diagnosis or appropriate rehabilitation upon completion of treatment
- The right to nutritional security or food supplements if needed to meet treatment requirements

Patients' Responsibilities

Patients have the responsibility to:

Share Information

- The responsibility to provide the health care giver as much information as possible about present health, past illnesses, any allergies and any other relevant details
- The responsibility to provide information to the health provider about contacts with immediate family, friends and others who may be vulnerable to tuberculosis or may have been infected by contact

Follow Treatment

- The responsibility to follow the prescribed and agreed treatment plan and to conscientiously comply with the instructions given to protect the patient's health, and that of others
- The responsibility to inform the health provider of any difficulties or problems with following treatment or if any part of the treatment is not clearly understood

Contribute to Community Health

- The responsibility to contribute to community well-being by encouraging others to seek medical advice if they exhibit the symptoms of tuberculosis
- The responsibility to show consideration for the rights of other patients and healthcare providers, understanding that this is the dignified basis and respectful foundation of the tuberculosis community

Show Solidarity

- The moral responsibility of showing solidarity with other patients, marching together towards cure
- The moral responsibility to share information and knowledge gained during treatment and to pass this expertise to others in the community, making empowerment contagious
- The moral responsibility to join in efforts to make the community tuberculosis free

Appendix III-C

NEW YORK CITY DEPARTMENT OF HEALTH AND MENTAL HYGIENE
BUREAU OF TUBERCULOSIS CONTROL

AGREEMENT FOR DOT IN THE FIELD

Date: _____

Between _____ and _____
Network Patient/Guardian

PATIENT SECTION

It has been explained to me that the most effective way to treat tuberculosis is by providing medication to the patient and having a trained health care worker observe the ingestion of all oral medication and verify the administering of injectables. Therefore, I _____ , agree to the following:
Patient

1. I will take my treatment under direct observation (DOT) and will keep all my DOT appointments.

2. I will attend all scheduled appointments on time at my doctor's office until my physician tells me that my treatment is complete.

_____ _____ _____
MD Name Address Phone #

2a. It has been determined by my physician that I will initially be taking medication _____ times a week. It has been explained to me that only my physician can change my medication and that all changes will be sent in writing to the _____ .
Field Office

3. If, for any reason, I cannot go to a scheduled physician appointment, I will **notify my DOT observer** and try to reschedule my visit.

3a. I will inform my DOT observer in advance of planned vacations and other appointments, and also if my address or telephone number changes.

4. I agree to comply with DOT visits at the mutually agreed upon place _____ and time frame _____.

4a. If I cannot meet the DOT observer at the above agreed upon place and time frame, I will contact DOT at:

_____ Central Phone

_____ DOT Observer Pager

5. If I have any questions, concerns, suggestions or complaints about any aspect of my care, I will tell

_____ _____
Name/Title Phone #

TB 314 (Rev. 11/02) Field DOT Agreement

STAFF SECTION

I, _____ , agree to the following:
DOT Assignee

1. I will assist the patient in maintaining his/her appointments.

2. I will respond to all questions and concerns raised by the patient and assist with referral for social services, to the best of my capacity.

3. I will ensure patient confidentiality to the best of my ability.

4. Occasionally, DOT observer and schedule may change and if so, the patient will be notified as quickly as possible.

5. I will ensure that your treating physician will receive a copy of this Agreement.

_____	_____	_____
Signature of Patient	Signature of DOT Observer	Signature of Supervisor

Appendix III-D

NEW YORK CITY DEPARTMENT OF HEALTH AND MENTAL HYGIENE
BUREAU OF TUBERCULOSIS CONTROL

AGREEMENT FOR DOT IN THE CHEST CENTER

Between _____ Chest Center and
Name of Center

_____ on this date _____
Name of Patient Today's Date

PATIENT SECTION

It has been explained to me that the most effective way to treat tuberculosis is by providing medication to the patient and having a trained health care worker observe the ingestion of all oral medication and verify the administering of injectables.

Therefore, I _____ , agree to the following:
Name of Patient

1. I agree to have my treatment given under direct observation (DOT) and keep all my DOT appointments.
2. I will attend all scheduled appointments on time at the _____
Name of Center
Chest Center until my physician tells me that my treatment is complete.
3. If, for any reason, I cannot go to a scheduled appointment, I will call
_____ at (_____) _____ to reschedule.
Name of Person to call Telephone Number

3a. I will inform DOT staff in advance of planned vacations and other appointments and if my address or telephone number changes.

4. If I have any questions, concerns, suggestions or complaints about any aspect of my care, I will tell
_____ or _____ .
Name of Person to Notify Name of Person to Notify

CHEST CENTER STAFF SECTION

Therefore, I _____ , agree to the following:
Name of Case Manager/DOT Observer

1. I will observe all the treatment and ask questions about how the patient is doing.

2. I will ensure that the patient is given free medications and reimbursed for all transportation to and from every center visit,

3. I will respond to all questions and concerns raised by the patient and assist with referral for social services, to the best of my capacity.

4. I will assist the patient in maintaining his/her appointments.

Therefore, I _____ , agree to the following:
Name of Treating Physician

1. I will ensure that the patient is being treated with the most advanced and effective therapy known to the medical profession.

2. I will inform and respond to questions from both the patient and case manager of all relevant medical information concerning the patient's progress, as permitted by the patient.

Signature of Patient	Signature of Case Manager/DOT Observer	Signature of Treating Physician

Appendix III-E

THE CITY OF NEW YORK
DEPARTMENT OF HEALTH AND MENTAL HYGIENE

Michael R. Bloomberg
Mayor

Thomas R. Frieden, M.D., M.P.H.
Commissioner

nyc.gov/health

Instructions for patients with potentially infectious TB

You are being discharged from the hospital although your sputum tests indicate that you may still infect other people with TB or you are advised to be evaluated as an outpatient while you may have infectious TB.

You are being discharged because you said that either you live alone or will be going back to a living arrangement where the other people living there are healthy and wish to have you home. We are required by law to notify them that they have been exposed to TB and to evaluate them.

You may have been placed on medication to treat TB already or are waiting to start medications after you have been evaluated as an outpatient.

The following instructions will help reduce the spread of TB germs to other people and you should follow them carefully:

- If you return to a home that has other people, you should always:
  - Limit the time spent in common household areas (such as bathroom or kitchen) and keep your bedroom door closed
  - Wear a surgical mask when spending time in a space that is also used by others to reduce the number of TB germs that you put in the air when you cough or talk.
- You should always cover your mouth when coughing or sneezing
- You should not be around infants, young children or, to the best of your knowledge, persons who have weakened immunity such as people with HIV/AIDS. (If there are young children at home, you may still be discharged to the home if the children have been evaluated for latent TB infection and are on "preventive" medication, as determined by their physician)
- You should participate in a program of directly observed therapy (DOT), about which you have been educated by an employee of the NYC health department
- You should avoid going to public places or return to work or school until your doctor, working with the health department, says it is OK for you to do so
- You should keep your doctor's or clinic appointments to ensure that treatment for TB is not interrupted
- Some of these restrictions will be removed once your physician, along with the health department, determines that you are no longer infectious
- Your TB treatment and DOT will continue even after these restrictions are removed.

Following these instructions will help in limiting the spread of TB germs to your family and others. If you have questions about your treatment please call your physician or health department at 311.

You can also find more information about TB on our website at nyc.gov/health/tb.

Appendix III-F

THE CITY OF NEW YORK
DEPARTMENT OF HEALTH AND MENTAL HYGIENE
Michael R. Bloomberg
Mayor
Thomas R. Frieden, M.D., M.P.H.
Commissioner
nyc.gov/health

Information for persons who live with patients with TB

A family member or someone in your household was recently diagnosed with or is suspected of having active TB. TB is a preventable and treatable disease. TB is transmitted through the air when a patient with the disease coughs or sneezes without covering his or her mouth. People with the active form of the disease must take their medication and must follow certain rules to prevent the spread of TB germs to people they live or work with. ***We are required by state law to inform you of this information.***

If there are children in your home they should be evaluated by their doctor and they should be placed on "preventive" therapy if appropriate. They can also be evaluated and treated at the health department's chest centers.

If a family member or someone in your household has been diagnosed with TB:

- You should get tested to see if you have already been infected with the germs that cause TB
- If you have been infected with the germs that cause TB, you should have a medical evaluation and a chest x-ray to make sure that you have not progressed to active TB
- If you have TB infection, you should take medicine to prevent the development of active TB.
- **The member of your household with TB should stay at home until his or her physician and the health department says he/she can go out.**
- He/she should not go to work or school during this time period and should avoid going to any public areas during this time period.
- Please assist the TB patient by doing their errands, such as grocery shopping.
- Your household member with TB should cover his/her mouth with a tissue whenever he/she coughs or sneezes; he/she should put the used tissue in the regular garbage.
- When around other people, the patient should wear a surgical mask that covers the nose and mouth.
- While at home, limit your contact with the TB patient as much as possible; the patient should sleep in a separate room until advised by their physician.
- It is OK to share eating utensils (spoons, forks, cups or glasses) and other household items.

Following these instructions will help in limiting the spread of TB germs to your family and others.
If you have questions about your treatment please call your physician or health department at 311.
You can also find more information about TB on our website at nyc.gov/health/tb.

Appendix III-G

THE CITY OF NEW YORK
DEPARTMENT OF HEALTH AND MENTAL HYGIENE
Michael R. Bloomberg
Mayor
Thomas R. Frieden, M.D., M.P.H.
Commissioner
nyc.gov/health

HOME ISOLATION PATIENT AGREEMENT

I _____, acknowledge that I have active infectious tuberculosis,
(Patient's full name)
and that I must separate myself from others in order to prevent other from being exposed to my tuberculosis disease. I have discussed this agreement with _____
(Full name of DOHMH employee)
a _____ at the Department of Health and Mental Hygiene
(Job title)
(DOHMH), who has answered my questions about home isolation fully to my satisfaction. I further acknowledge that if I am unable or unwilling to observe any of the conditions of this agreement, while my tuberculosis remains infectious, I represent a danger to the health of others and I am subject to removal to a hospital for respiratory isolation either voluntarily or by order of the Commissioner of Health.

In return for being allowed to remain in my home while my tuberculosis is infectious, I agree to all of the following conditions.

- I will take all my prescribed anti-tuberculosis medications in a program of daily directly observed therapy (DOT) as directed by my physician or the Commissioner of Health.
- I will entertain no visitors in my home and will not visit other persons' home.
- I will cover my mouth and nose whenever I cough, sneeze, or hack while indoors or outdoors in the presence of other people.
- I will not use any public (bus, train, taxi, subway, airplane) or private (automobile) transportation unless absolutely necessary to obtain medical attention, and then only using the mask which my physician has prescribed for me.
- I will not visit enclosed public spaces such as theaters, shopping malls, department, supermarket or other stores; but I may spend time in open spaces such as parks, backyards or public streets which are not crowded.
- I will not care for or spend time with children of any age or work outside my home without permission from my physician and the DOHMH.
- I will not leave New York City for any reason without the DOHMH and my physician's permission and under such conditions as are prescribed.
- I have received a copy of the instructions entitled "Instructions for Patients with Potentially Infectious TB"
- Any additional conditions:

_____
_____
_____

If I have any further questions about how to comply with this agreement, I will telephone
_____ at _____
(Full name and title of contact person at DOHMH) (Telephone number with area code)

Date: _____ _____
(Patient's signature)

Date: _____ _____
(Staff signature)

Revised: July 2006

International Classification of Tuberculosis

Class	Type	Description
0	No TB exposure Not infected	No history of exposure Negative test for TB infection[1,2]
I	TB exposure No evidence of infection	History of exposure Negative test for TB infection[1,2]
II	TB infection No disease	Positive test for TB infection[1,2] No clinical or radiographic evidence of TB Negative bacteriologic studies (if done)
III	Current TB disease	Positive culture for *M. tuberculosis* and/or Clinical or radiographic evidence of current TB disease, with or without a positive test for TB infection[1,2]
IV	Previous TB disease	History of episode(s) of TB or Abnormal but stable radiographic findings, positive test for TB infection[1,2], no clinical or radiographic evidence of current TB disease and negative bacteriologic studies (if done)
V (High)[3]	Current TB disease suspected	Diagnosis pending, but expected to evolve as Class III
V (Low)[3]	Previous TB disease suspected	Diagnosis pending, but expected to evolve as Class IV or as an abnormality not related to TB

Adapted from CDC. *Core Curriculum on Tuberculosis, Third Ed.* Atlanta: Centers for Disease Control and Prevention; 1994

[1] Whether a tuberculin skin test reaction is classified as positive or negative depends on the TB risk factors of the person being tested. For guidelines on classifying the skin test reaction, see p.179 of this manual.

[2] Tests for TB infection are either a tuberculin skin test or a blood-based assay.

[3] The division of Class V into "high" and "low," intended to improve case management, is specific to the New York City Department of Health and Mental Hygiene; it is not part of the International Classification.