

II. SCREENING AND TESTING FOR INFECTION

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1. STANDARDS OF PUBLIC HEALTH PRACTICE

- II-1. The TB Risk Assessment Tool (TB RAT) is completed prior to testing for TB infection.
- II-2. Testing for TB infection is performed only if the individual is dispositioned as “high-risk” for TB infection or for progression to TB disease if infected according to the TB RAT.
- II-3. High-risk contacts to infectious TB cases are tested for TB/HIV co-infection unless they specifically “opt-out” of HIV testing.

2. TERMINOLOGY

In this document and related modules of the *TTBEP* Manual, the term “TB Infection (TBI)” has been substituted for the term “latent TB infection (LTBI)” which appears in guidelines developed by the American Thoracic Society (ATS) and the Centers for Disease Control and Prevention (CDC). The rationale for this change is that recent research strongly suggests that the absence of evidence for active TB through traditional diagnostic techniques cannot definitively exclude the presence of subclinical and progressive TB disease in persons infected with *Mycobacterium tuberculosis*. References from the medical literature describing this evolving understanding of the spectrum of TB infection and TB disease are available from TTBEP Central Office (C.O.) upon request.

Much confusion exists in the terminology used to describe the result of the tuberculin skin test (TST). For that reason, TTBEP makes the following distinctions in terminology in this document:

“Reading the TST” refers to these activities:

- Detecting any induration at the TST site (induration present = “reactive”; induration not present = “non-reactive”); and
- Measuring and recording the transverse diameter of any induration in millimeters (mm).

“Interpreting the TST” refers to determining the significance of any induration present based upon CDC-defined risk categories for TB infection (**Refer to Table II-3**):

- No induration or <5 mm = “Negative”
- 5+ mm, 10+ mm, or 15+ mm based upon risk category = “Positive”

“Result of the TST” is the documented interpretation of the TST measurement as “Negative” or “Positive.”

3. SCREENING

Risk of TB Exposure

A strategic component of tuberculosis control is to identify persons at high risk for developing TB who would benefit by treatment of TB infection (TBI), if detected.

Table II-1 identifies persons with increased risk* for TB Infection.

Table II-1: Risk Factors for *Mycobacterium tuberculosis* Infection

<ul style="list-style-type: none"> • Close contacts of persons known or suspected to have active tuberculosis 	<ul style="list-style-type: none"> • Foreign-born persons from areas that have a high incidence of active tuberculosis (e.g., Africa, Asia, Eastern Europe, Latin America, and Russia)
<ul style="list-style-type: none"> • Persons who visit areas with a high prevalence of active tuberculosis, especially if visits are frequent or prolonged (for testing information on these individuals Refer to Table IX-1 in Module IX. Targeted Testing in Populations at High-Risk) 	<ul style="list-style-type: none"> • Residents and employees of congregate settings whose clients are at increased risk for active tuberculosis (e.g., correctional facilities, long-term care facilities, and homeless shelters), etc.
<ul style="list-style-type: none"> • Health-care workers who serve clients who are at increased risk for active tuberculosis 	<ul style="list-style-type: none"> • Populations defined locally as having an increased incidence of <i>M. tuberculosis</i> infection or active tuberculosis, possibly including medically underserved, low-income populations, or persons who abuse drugs or alcohol§
<ul style="list-style-type: none"> • Infants, children, and adolescents exposed to adults who are at increased risk for <i>M. tuberculosis</i> infection or active tuberculosis 	

*Persons with these characteristics have an increased risk for *M. tuberculosis* infection compared with persons without these characteristics.

§There is no standard definition for “excess alcohol use.”

Excess alcohol use can be assessed by various methods, such as the following:

- Participation in self-help programs (e.g., Alcoholics Anonymous) or alcohol treatment programs
- Medical documentation of excess alcohol use or hospitalization for alcohol-related medical conditions (e.g., delirium tremors [DTs], pancreatitis, cirrhosis)
- More than one arrest for intoxication or drunk or disorderly behavior. This can be ascertained by asking the patient, or contacting the local correctional facility regarding charges

The National Household Survey on Drug Abuse defines heavy alcohol use as “five or more drinks on the same occasion on each of 5 or more days in the past 30 days.” Numerous screening instruments (e.g., CAGE, AUDIT, MAST) can be helpful in identifying persons who may use alcohol to excess.

A standard drink in the United States is equal to 13.7 grams (0.6 ounces) of pure alcohol, or

- 12 ounces of beer
- 8 ounces of malt liquor
- 5 ounces of wine
- 1.5 ounces or a “shot” of 80-proof distilled spirits or liquor (e.g., gin, rum, vodka, or whiskey)

<http://www.cdc.gov/tb/programs/rvct/InstructionManual.pdf>

Excessive drinking includes binge drinking (four or more drinks on an occasion for women, five or more drinks on an occasion for men); consuming eight or more drinks a week for women or 15 or more drinks a week for men; or any alcohol use by pregnant women or those under the minimum legal drinking age of 21. (<http://www.cdc.gov/media/releases/2014/p1120-excessive-drinking.html>).

Reference:

1. CDC. Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection. MMWR 2000; 49 (No. RR-6). <http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf> (adapted)

Risk of Progression to TB Disease

The following is a list of persons who, if infected, would be at increased risk* for progression to TB disease (**Refer to Table II-2**).

Table II-2: Risk Factors for Progression of Infection to Active Tuberculosis

<ul style="list-style-type: none"> • Persons with human immunodeficiency virus (HIV)[†] 	<ul style="list-style-type: none"> • Infants and children aged <5 years[†]
<ul style="list-style-type: none"> • Persons who are receiving immunosuppressive therapy such as tumor necrosis factor-alpha (TNF-α) antagonists, systemic corticosteroids equivalent to ≥ 15 mg of prednisone per day or immune suppressive drug therapy following organ transplantation[†] 	<ul style="list-style-type: none"> • Persons with a history of untreated or inadequately treated active tuberculosis, including persons with fibrotic changes on chest radiograph consistent with prior active tuberculosis
<ul style="list-style-type: none"> • Persons who were recently infected with <i>M. tuberculosis</i> (within the past 2 years) 	<ul style="list-style-type: none"> • Persons who have had a gastrectomy or jejunioileal bypass
<ul style="list-style-type: none"> • Persons with silicosis, diabetes mellitus, chronic renal failure, leukemia, lymphoma, or cancer of the head, neck or lung 	<ul style="list-style-type: none"> • Persons who weigh <90% of their ideal body weight
<ul style="list-style-type: none"> • Populations defined locally as having an increased incidence of active tuberculosis, including medically underserved or low-income populations 	<ul style="list-style-type: none"> • Cigarette smokers and persons who abuse drugs or alcohol

* Persons with these characteristics have an increased risk for progression of infection to active tuberculosis compared with persons without these characteristics.

[†] Indicates persons at increased risk for a poor outcome (e.g., meningitis, disseminated disease, or death) if active tuberculosis develops.

References:

1. CDC. Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection. MMWR 2000; 49 (No. RR-6). <http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>
2. CDC. Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection—United States, 2010. MMWR 2010; 59 (No. RR-5). <http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf>
3. Current TTBEF TB Risk Assessment Tool and Instructions
4. Current TB Nursing Protocol

Assessment of Symptoms

All patients being evaluated for TBI or TB disease must be assessed for symptoms of active TB disease. This information is documented on the TB Risk Assessment Tool (TB RAT).

The general (systemic) symptoms of TB disease may include but are not limited to:

- Unexplained weight loss

- Loss of appetite
- Night sweats
- Fever
- Fatigue
- Chills

The symptoms of TB disease of the lungs may include:

- Cough lasting \geq 2-3 weeks
- Hemoptysis (coughing up blood)
- Shortness of breath
- Chest pain

Other symptoms depend on the part of the body that is affected, and TB disease may affect any organ system.

The TB Risk Assessment Tool

In Tennessee, the Tuberculosis Risk Assessment Tool (TB RAT) (PH 3714) (**Appendix A**) is:

- An interview guide and documentation tool for use by public health staff
- Used to determine a patient’s risk for TB infection or progression to TB disease if infected
- Required to guide decision-making about testing for TBI

The TB Risk Assessment Tool (TB RAT) is completed prior to testing for TB infection (**Standard of Public Health Practice II-1**).

Routine testing is not recommended for populations found to be at “low-risk” for TBI or TB disease except in certain circumstances (**Refer to the Appendix B for TB RAT instructions and also refer to current PHN Nursing Protocol**). Testing of “low-risk” occupational groups for administrative purposes is discouraged. Persons requesting testing who are dispositioned as “low-risk” according to the TB RAT, should be provided a letter stating that the patient is low-risk and was not tested (**Refer to Appendix U**).

The following persons should be screened with the TB RAT:

- Anyone with TB symptoms or with TB infection risk factors
- All persons with suspected or confirmed TB disease
- All contacts to a person with suspected or confirmed TB disease
- All foreign-born individuals from TB-endemic countries (**Refer to current TB Nursing Protocol for list of TB-endemic countries**)
- Persons referred for a positive TST or IGRA placed outside of the health department
- Anyone who would benefit from TB education and individualized assessment (i.e., a patient who may have risk of TB infection)
- Any person who, if infected, would be at high risk for progression to TB disease

Testing for TB infection is performed only if the individual is dispositioned as “high-risk” for TB infection or for progression to TB disease if infected according to the TB Risk Assessment Tool (TB RAT) (**Standard of Public Health Practice II-2**).

References:

1. CDC, Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection. MMWR 2000; 49 (No. RR-6). <http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>
2. CDC, Updated guidelines for Using Interferon Gamma Release Assays to detect Mycobacterium tuberculosis Infection – United States. MMWR 2010; 59 (No. RR-5). <http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf>

Testing with Intention to Treat

In public health clinics in Tennessee, the decision to administer a TB test (IGRA or TST) is a decision to:

- Fully assess the patient
- Consider treatment of TBI if the
 - TB test result is positive
 - Patient is immunocompromised, regardless of the TB test result
 - Patient is a “high-risk” TB contact
- Assure follow-up of the patient until treatment completion

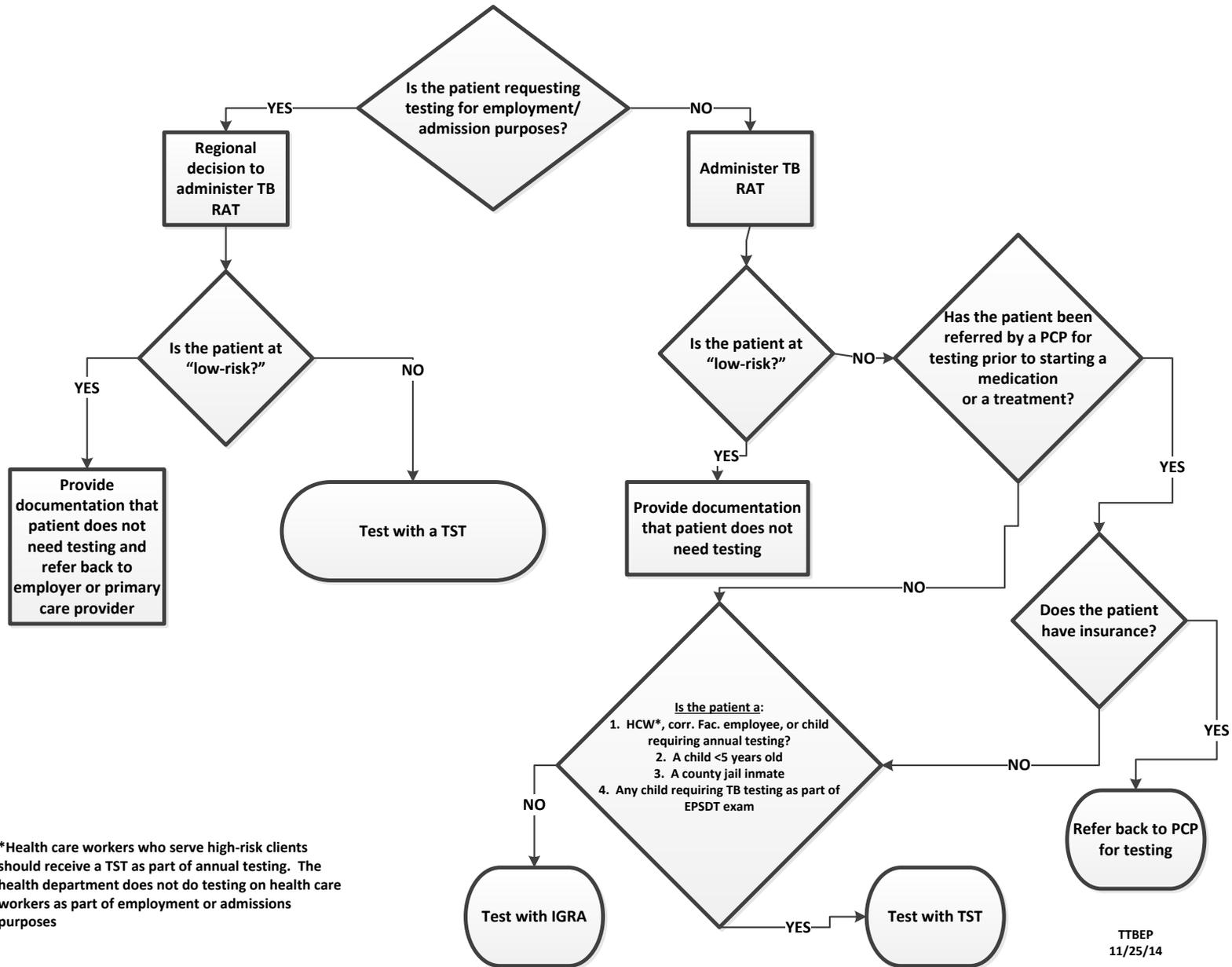
Testing is discouraged unless a plan is in place to complete a course of treatment in persons found to have TBI. The plan should include:

- Arrangements for medical evaluation
 - Chest X-ray (CXR)
 - Physical exam
- Monthly assessments at the health department

4. TESTING FOR TB INFECTION

Figure II-1 shows the algorithm for TB testing.

Figure II-1: TB Testing Algorithm



Mantoux Tuberculin Skin Test (aka “TST”)

Facts about the TST

- The TST is used to determine if a person is infected with *M. tuberculosis*.
- The substance used for the TST is called “purified protein derivative” (PPD), which is derived from tuberculin.
- Tuberculin skin testing with intermediate strength (5 TU (Tuberculin Units)) PPD, administered by the Mantoux intradermal technique, is the only currently recommended method; multiple-puncture tests should never be used.
- PPD produces a T-cell mediated delayed-type hypersensitivity reaction if the person has been infected with *M. tuberculosis*.
- It takes two to eight (2 to 8) weeks after initial infection with *M. tuberculosis* for the immune system to be able to react to PPD and for the infection to be detected by the TST.
- TST may be administered when a risk factor is identified, beginning at 3 months of age.
- TST is not contraindicated for pregnant or breastfeeding persons.
- Use “two-step TST” process to ascertain a reliable baseline TB status for persons who are required to receive serial testing for TB infection (refer to current TB Nursing Protocol).
- A history of vaccination with Bacillus Calmette-Guérin (BCG) is not a contraindication for testing with the TST or IGRA. Administer and measure the TST in BCG-vaccinated persons using the same technique as for persons with no previous BCG vaccination.
- Vaccination with live viruses may interfere with TST reactions. For persons scheduled to receive a TST, testing should be done as follows:
 - Either on the same day as vaccination with live-virus vaccine or four to six (4-6) weeks after the administration of the live-virus vaccine
 - At least one month after smallpox vaccination

Storage and Administration Precautions for Purified Protein Derivative (PPD) Solution

- Storage precautions for PPD antigen:
 - Date each vial when opened and discard unused portions of opened PPD vials after 30 days or upon expiration date.
 - Keep PPD vials refrigerated at all times (36-46°F)
 - May be placed in a cooler with ice packs to maintain temperature.
 - Discard if frozen.
 - Keep PPD vials protected from light and heat
 - If the vial is exposed to light or heat for an extended or unknown period of time, discard appropriately.
- Administration precautions for PPD antigen:
 - Never transfer PPD antigen from one vial to another vial.
 - Do not draw up the PPD antigen into syringe until ready to administer the TST, to prevent possible interaction between the PPD solution and the plastic syringe. Skin tests should be given immediately after the syringe has been filled.

- Avoid injecting PPD antigen subcutaneously, as a general febrile reaction or acute inflammation may occur.

NOTE: The packaging of tetanus toxoid-containing vaccine appears similar to Tubersol® and Aplisol® and all are refrigerated. Ensure that the correct solution (tuberculin) is used to place the TST.

Reference:

1. Tuberculin Purified Protein Derivative (Tubersol®) package insert

Eligibility Requirements

Persons who are determined to be at “high-risk” on the TB RAT are eligible to receive a TB test (TST/IGRA) per the current TB Nursing Protocol.

Exclusion Criteria

If patient has had a prior severe reaction or allergy to the tuberculin, the TST should not be given. Follow current TB Nursing Protocol.

Placing the TST

Supplies and Equipment

- PPD antigen, Tween-Stabilized (Tubersol®) is preferred
- Tuberculin syringe, 1.0 or 1/2 cc., with 25-gauge needle, disposable (one for each patient tested). The type of syringe utilized may change as new syringe/needle units become available
- Antiseptic (alcohol) and millimeter ruler

Procedure

- Follow universal recommendations for infection control. Gloves can be worn during the procedure and care should be taken to avoid contact with the patient’s blood. Do not recap, bend or break needles, or remove needles from the syringe.
 1. The TB skin test is given in the volar (palm side) surface of the left forearm, 2 to 4 inches below the elbow; the scapula area may be used as an alternative site for persons who cannot receive the TB skin test in the lower arm.
 2. Cleanse injection site with alcohol sponge.
 3. Cleanse vial stopper of antigen with a new alcohol sponge and insert needle into inverted bottle.
 4. Withdraw 0.1 ml (excluding air bubbles) of 5 tuberculin units (TU) of PPD and have the lumen of the needle filled.
 5. Hold syringe horizontal to arm with the bevel of the needle pointing upward.
 6. Before injecting, the skin can be tightened by grasping the underpart of the forearm and exerting pressure downward.
 7. With the needle bevel against the patient’s skin, insert it slowly at a 5 to 15 degree angle, between the layers of the skin.

8. Slowly inject the tuberculin solution. A tense, pale wheal (elevation of the skin) 6-10 mm in diameter, should appear over the needle bevel. The wheal should be at least 6 mm in diameter. If the wheal is less than 6 mm in diameter, the test should be repeated at a different site, at least 2 inches (50mm) from the original site or an alternate placement site. Document to indicate this alternate site. To ensure proper administration of TST, use the millimeter ruler to immediately measure the wheal at its maximum size.
9. Remove the needle without pressing or massaging the area. Do not cover the TST site with an adhesive bandage. Instruct the patient not to rub or scratch the site.
10. Schedule an appointment for patient to return for reading of the TST in 48-72 hours. NOTE: TSTs should not be placed on a Thursday unless the test reaction site can be measured over the weekend by a qualified/trained person.

Reading the TST

- Tests should be read between 48 and 72 hours after placement, when the induration (hard, dense, raised formation) is maximal.
 - Tests read after 72 hours tend to underestimate the true size of induration, thus patients with a TST reaction measurement that does not meet the appropriate criteria for positivity when measured after more than 72 hours must be retested.
 - A reaction that meets the criteria for TST positivity and is measured more than 72 hours after TST placement may still be interpreted as “positive.”
 - In no case should a TST reaction be considered valid if read more than 1 week following TST placement.
- TST reading should be performed in a good light, with the forearm slightly flexed at the elbow.
- The basis of reading the TST is the presence or absence of induration, which may be determined by inspection (from a side view against the light as well as by direct light) and by palpation.
- Use fingertips to find margins of raised induration, marking the widest edges of induration across forearm.
- For standardization, the diameter of induration should be measured transversely (across) to the long axis of the forearm. Observer variability may be decreased by using the ball-point pen method to measure induration (drawing until pen stops at induration).

NOTE: Erythema (reddening of the skin) alone is not indicative of a positive test and should not be measured or recorded.

Interpreting the TST Result

Interpretation of TST reaction depends on two factors: (1) the measurement (in millimeters) of induration, and (2) the risk category of the individual for acquiring TB infection or the risk of progression to TB disease if infected. CDC has established three risk categories for this purpose,

each of which has a different measurement threshold (i.e., “cut point”) to determine whether the skin test reaction is interpreted as “positive” or “negative.” A person with a “positive” reaction should be referred for a medical evaluation for TB infection (TBI) and disease and appropriate follow-up and treatment if necessary. A measurement of 0 mm, or a measurement below the defined cut-point for the appropriate risk category, is considered “negative” (Refer to Table II-3). A negative TST or IGRA result does not exclude the diagnosis of TB infection or active TB disease.

Table II-3: Interpreting the TST Reaction

5 or more millimeters	10 or more millimeters	15 or more millimeters
<p>An induration of 5 or more millimeters is considered positive for</p> <ul style="list-style-type: none"> ▪ HIV- infected persons ▪ Recent contacts of persons with infectious TB ▪ People who have fibrotic changes on a chest x-ray ▪ Patients with organ transplants and other immunosuppressed patients (including patients taking a prolonged course of oral or intravenous corticosteroids or TNF-α antagonists) 	<p>An induration of 10 or more millimeters is considered positive for</p> <ul style="list-style-type: none"> ▪ People who have come to the US within the last 5 years from areas of the world where TB is common (e.g., Asia, Africa, Eastern Europe, Russia, or Latin America) ▪ Injection drug users ▪ Mycobacteriology lab workers ▪ People who live or work in high-risk congregate settings ▪ People with certain medical conditions that place them at high risk for TB (silicosis, diabetes mellitus, severe kidney disease, certain types of cancer, and certain intestinal conditions) ▪ Children <5 years ▪ Infants, children, and adolescents exposed to adults in high-risk categories 	<p>An induration of 15 or more millimeters is considered positive for</p> <ul style="list-style-type: none"> ▪ People with no known risk factors for TB

Reference:

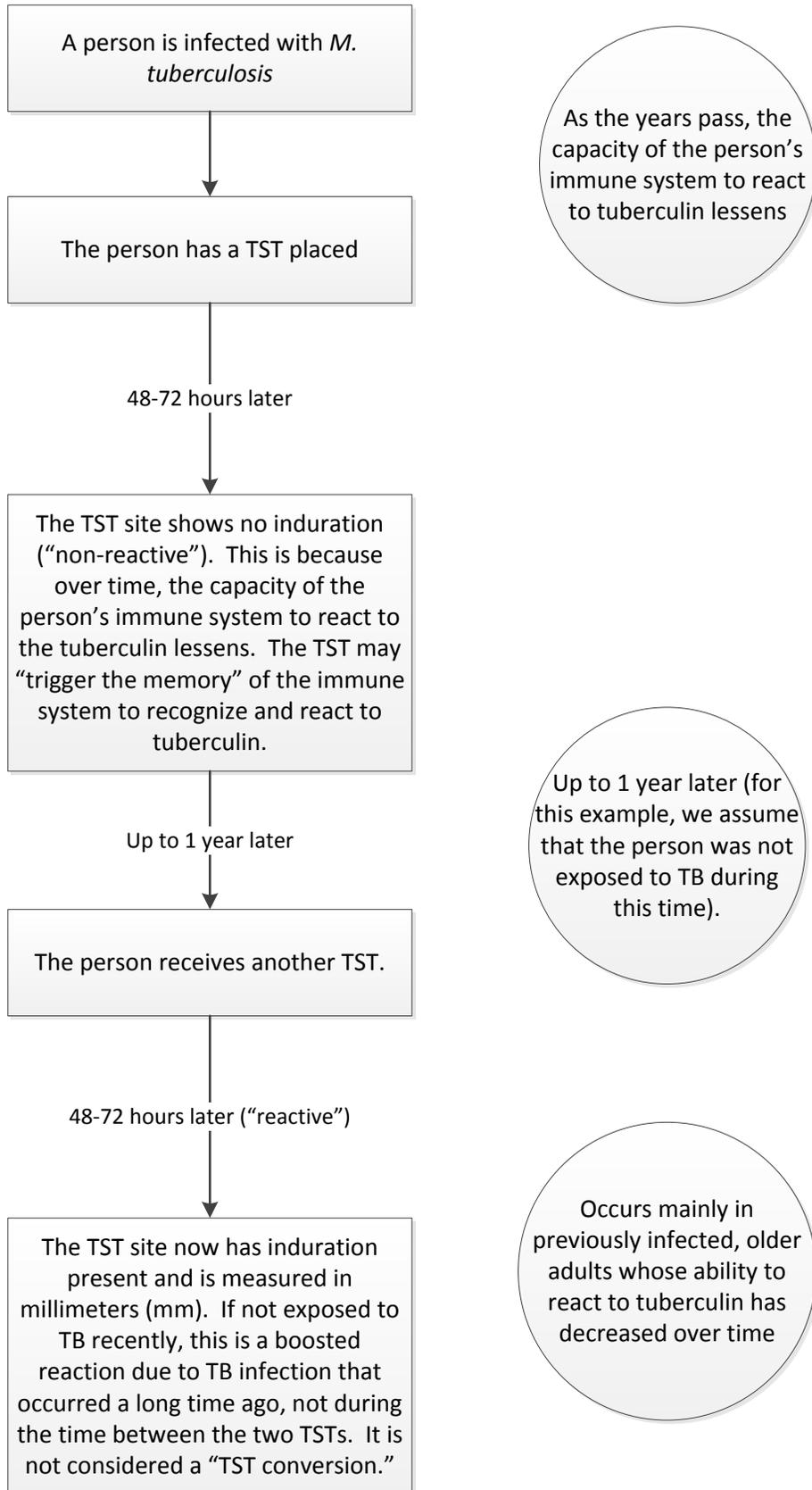
1. CDC. Core Curriculum on Tuberculosis: What the Clinician Should Know. 2013. <http://www.cdc.gov/tb/education/corecurr/default.htm>

Booster Reaction

The booster phenomenon occurs mainly in previously infected, older adults whose immune system capacity to react to tuberculin has waned over time. When these people are skin tested many years after they were infected with *M. tuberculosis*, they may have an initial negative reaction. However, if they are tested again within a year of the first test, they may have a positive reaction. This is because the first TST “triggered the memory” of the immune system, boosting its capacity to react to the second TST. It may appear that these people were infected between the first and second tests (recent TB infection). However, unless there has been an exposure to infectious TB in the interim, the second result now read as reactive is actually a boosted reaction due to TB infection that occurred a long time ago. These people may still be considered for TBI treatment if they fit into a high-risk category for progression to TB disease.

Figure II-2 describes the boosting reaction.

Figure II-2: Interpretation of a Booster Reaction



Reference:

1. CDC. Core Curriculum on Tuberculosis: What the Clinician Should Know. 2013. <http://www.cdc.gov/tb/education/corecurr/default.htm> (adapted)

Several factors can lead to false-positive or false-negative skin test reactions (**Refer to Table II-4**).

Table II-4: Interpreting False-Positive and False-Negative Reactions to the TST

Type of Reaction	Possible Cause	People at Risk
False - positive	Non-tuberculous mycobacteria (NTM)	People infected with NTM
	BCG vaccination	People vaccinated with BCG
	Administration of incorrect antigen	Any person being tested
	Incorrect interpretation of TST result	Any person being tested
False - negative	Anergy	HIV-infected people, other people with weakened immune systems, severe TB disease, and some viral illness (e.g., measles, mumps, and chicken pox) or bacterial infection (e.g., typhoid, etc.)
	Recent TB infection	People infected with <i>M. tuberculosis</i> within the past 8 weeks
	Concurrent viral infection (measles, mumps, varicella)	People injected with a live-virus vaccination
	Concurrent bacterial infection	People with typhoid fever, brucellosis, typhus, leprosy, pertussis
	Concurrent fungal infection	People with fungal infection
	Chronic renal failure	People with renal failure
	Low protein states	People with severe protein depletion afibrinogenemia
	Diseases affecting lymphoid organs	People with Hodgkin's disease, lymphoma, chronic leukemia, sarcoidosis
	Immunosuppressive drugs	People taking medical steroids, TNF-alpha blockers or comparable drugs
	Very young or elderly persons	Newborns < 6 months of age or elderly patients with immature or waning immunity
	Stress	People who have had surgery, burns, mental illness, graft-versus-host reactions
	Incorrect storage or handling of antigen, incorrect administration of the TST, or results that are not measured or interpreted properly	Any person being tested

Reference:

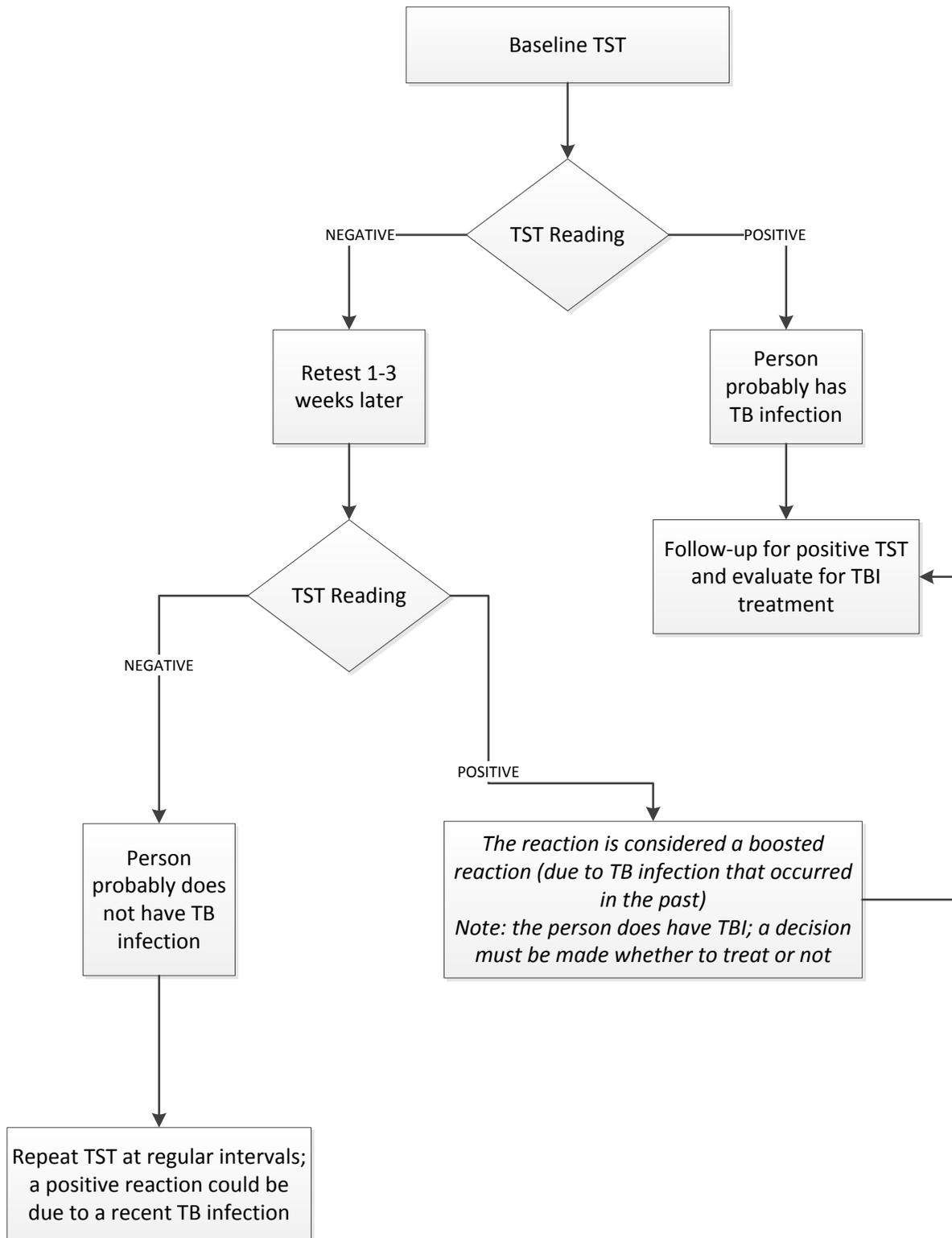
1. CDC. Core Curriculum on Tuberculosis: What the Clinician Should Know. 2013. <http://www.cdc.gov/tb/education/corecurr/default.htm> (adapted)

Two-Step Method (for serial TB testing only)

- Giving a second TST after an initial negative TST reaction is called “two-step testing.”
- Two-step testing is done to detect waning sensitivity to infection with *Mycobacterium tuberculosis*. This method is used in initial skin testing of adults who will be tested periodically, such as health care workers. This test distinguishes a boosted reaction (caused by TB infection that occurred many years before the skin test) from a reaction caused by recently acquired TB infection.
- Administer a Mantoux Tuberculin Test using 5 TU (0.1 ml) PPD in the left forearm as previously described for TST placement.
- Measure and interpret the test reaction within 48-72 hours.
 - If the reaction to the first test is measured and interpreted as “negative,” a second TST should be repeated 1 to 3 weeks later.
 - If the second TST reaction is interpreted as “positive,” the result probably represents a boosted reaction.
 - On the basis of this second test result, the person should be:
 - Classified as previously infected (This result would not be considered a TST conversion or a new TB infection)
 - Be a candidate for TBI treatment with appropriate follow-up
- Two-step skin testing should not be repeated once a valid baseline result is established.

Figure II-3 describes the two-step TST testing method.

Figure II-3: Two-Step TST Testing



Documentation

- The person administering the test should record the date the test was placed and sign his/her initials.
- TST measurements should be recorded only in millimeters (mm) of induration. The absence of induration should be recorded as “0 mm,” not “negative.”
- Never record the TST result (i.e., measurement) as “positive” or “negative.”
- The person reading the test should record the date the test was read and initial next to the result.

Refer to the current TB Risk Assessment (TB RAT) Instructions (**Appendix B**) for further instructions on recording TST or IGRA results in PTBMIS.

Reference:

1. CDC. Core Curriculum on Tuberculosis: What the Clinician Should Know; 2013. http://www.cdc.gov/TB/education/corecurr/pdf/corecurr_all.pdf

Interferon-Gamma Release Assays (IGRA)

Two IGRAs have been approved by the Food and Drug Administration (FDA) since 2005—the QuantiFERON® -TB Gold In-Tube and T-Spot.TB® test. An IGRA may be used in place of (but not in addition to) a TST in all situations in which CDC recommends a TST as an aid in diagnosing *Mycobacterium tuberculosis* infection, with the preferences and specific considerations below:

- Preferred for testing persons from groups that historically have poor rates of return for TST reading.
- Preferred for testing persons who have received BCG (as a vaccine or for cancer therapy).
- Generally should not be used for testing children younger than 5 years of age unless used in conjunction with TST.
- May be used in place of TST to test recent contacts of persons with infectious TB disease with special considerations for follow-up testing:
 - IGRAs offer the possibility of detecting *M. tuberculosis* infection with greater specificity than with a TST;
 - Data on the ability of IGRAs to predict subsequent TB disease are limited;
 - If IGRAs are to be used in contact investigations, negative results obtained prior to 8 weeks typically should be confirmed by repeating the test 8 to 10 weeks after the end of exposure;
 - Use of the same test for repeat testing will minimize misclassification errors that occur due to test discordance.
- IGRAs do not boost subsequent test results and can be completed following a single patient visit.
- Routine testing with both a TST and IGRA is not recommended; however results from both tests may be useful in the following situations when the initial test is **negative**:

- When the risk of infection, the risk of progression from infection to disease, and the risk of a poor outcome are high (e.g., HIV infection, children under 5 years of age who are exposed to persons with infectious TB); or
- When there is clinical suspicion for TB disease (e.g., signs and symptoms of active TB, and/or radiographic evidence suggestive of TB disease) and confirmation of *M. tuberculosis* infection is desired.
- Routine testing with both a TST and an IGRA is not recommended; however, results from both tests may be useful in the following situations when the initial test is **positive**:
 - Additional evidence of infection is required to encourage compliance (e.g., foreign-born persons who believe their positive TST is due to BCG); and
 - In healthy persons who have a low risk of both infection and progression from TB infection to TB disease.
- Repeating an IGRA or performing a TST may be useful when the initial IGRA result is indeterminate, borderline, or invalid, and a reason for testing persists.
- Any person that has an indeterminate IGRA result is to be retested as soon as possible but no later than 14 days.
- If a TST was placed and a physician orders an IGRA, the IGRA must be drawn within three (3) days of the TST placement. If not drawn within three (3) days, the IGRA should be delayed two (2) months.
- In general, if a positive TST is to be confirmed with an IGRA, the testing should be done within three (3) days of the TST placement or the test should be delayed two (2) months
http://www.heartlandntbc.org/products/tb_at_a_glance.pdf.

Reference:

1. CDC. Core Curriculum on Tuberculosis: What the Clinician Should Know. 2013.
http://www.cdc.gov/tb/education/corecurr/pdf/corecurr_all.pdf
2. Heartland National TB Center. Tuberculosis at a Glance: A Reference for Practitioners on Basic Tuberculosis Information. 2nd Ed. 2010.
http://www.heartlandntbc.org/assets/products/tb_at_a_glance.pdf

Interferon-Gamma Release Assay (IGRA)-QuantIFERON[®]-TB Gold In-Tube

Uses

- “QuantIFERON[®]-Gold In-Tube” (QFT-GIT) is a laboratory test used for detecting infection with *Mycobacterium tuberculosis*. It is one specific FDA-approved test of a general type called “interferon-gamma release assays” (IGRA).
- The TTBEF utilizes the QFT-GIT assay in regional TB clinics and health departments in all counties across Tennessee.
- As with TST, live virus vaccines might affect IGRA test results. However, the effect of live virus vaccination on IGRAs has not been studied. Until additional information is available, IGRA testing in the context of live virus vaccine administration should be done as follows:

- Either on the same day as vaccination with live-virus vaccine or 4-6 weeks after the administration of the live-virus vaccine
- At least one month after smallpox vaccination

Table II-5 compares the benefits of test with QFT-GIT compared to a TST.

Table II-5: Benefits of QFT-GIT Compared to TST

TST	QFT-GIT
<ul style="list-style-type: none"> ● Patients must visit the clinic twice to have the TST. Failure to return to have the test result read necessitates having the patient return to have the TST re-administered 	<ul style="list-style-type: none"> ● QFT-GIT is performed in one visit
<ul style="list-style-type: none"> ● Previous vaccination with BCG can lead to a false-positive TST result in a patient who is not infected with <i>M. tuberculosis</i> 	<ul style="list-style-type: none"> ● QFT-GIT is not affected by BCG vaccination
<ul style="list-style-type: none"> ● False-positive TST results may occur in 3% to 65% of all persons tested depending upon prevalence of TB in the population 	<ul style="list-style-type: none"> ● QFT-GIT is >99% specific, virtually eliminating false-positive readings
<ul style="list-style-type: none"> ● An initial TST may cause future TSTs to be subject to boosting, resulting in increased potential for false-positive results 	<ul style="list-style-type: none"> ● QFT-GIT is not subject to boosting, eliminating the need for two-step testing

Reference:

1. CDC. Updated Guidelines for Using Interferon Gamma Release Assays to Detect Mycobacterium tuberculosis Infection—United States, 2010. MMWR 2010; 59 (No. RR-5). <http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf>

Eligibility Requirements

QFT-GIT should only be used to test individuals who are identified as at “high-risk” for TB infection and/or progression of TB infection to active TB disease as indicated through administration of the TB Risk Assessment Tool (TB RAT).

- **Refer** to the current TB Nursing Protocol
- **Refer** to TB Risk Assessment Tool Instructions (**Appendix B**)
- **Refer** to the current QuantiFERON Policy and Procedures (**Appendix C**)

Exclusion Criteria

The following people are excluded from testing with QFT-GIT:

- Children < 5 years old
- Any child, regardless of age, requiring TB testing as part of the Early and Periodic Screening, Diagnostic and Treatment (EPSDT) exam
- Any person determined to be “low-risk” through the TB RAT
- Health Care Workers (HCWs) and other individuals required by an employer or educational institution to have a baseline or serial TB test (e.g., annually) as a condition

of employment or enrollment. QFT-GIT should not be used for employment/admission testing or serial testing

- Routine testing of county jail inmates and jail employees in jurisdictions in which targeted TB testing is financially supported by the TTBEF

Opt-Out Testing for HIV Co-Infection

CDC recommends HIV testing for all patients being tested for TB. Assent by the patient is inferred unless the patient specifically declines HIV testing (i.e., “opt-out” testing).

- Routine HIV testing is recommended for persons suspected of having:
 - TB disease
 - TB infection
 - Contacts to persons with infectious TB disease
- Provider will discuss with the patient any reason given by the patient for declining the HIV test:
 - Lack of perceived risk
 - Fear of HIV/AIDS
 - Concern regarding partner violence
 - Potential stigma or discrimination
- Logistical reasons for not testing (e.g., scheduling) should be resolved

During blood draw for QFT-GIT with a “butterfly” needle, a “red-top” tube is to be used to purge the plastic line and set aside for the HIV test before collecting the QFT-GIT blood specimens. This process should be followed routinely as a part of patient evaluation.

Reference:

1. CDC. Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings, 2005. MMWR 2005; 54 (No. 17).
<http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf>

Specimen Collection and Handling

Equipment and supplies needed:

- Disposable gloves
- 1 standard 7ml “red-top” tube
- 3 QFT-GIT 1ml specimen tubes per patient test (1 red-top, 1 grey-top, 1 purple-top)
- Appropriate laboratory requisition
- Alcohol swabs
- Blood collection kit
- Tourniquet
- Dry gauze pad or cotton or rayon ball
- Adhesive bandage

Procedure

1. Complete an appropriate laboratory requisition form (i.e., paper requisition or lab order entry [LOE]).
2. Collect blood using a purge tube (standard 7ml red-top tube) followed by each of the three 1ml QFT-GIT blood collection tubes. QFT-GIT tubes are identified by a grey top ("NIL"), red top ("TB ANTIGEN"), and purple top ("MITOGEN"). NOTE: the red-top purge tube should be used for HIV screening unless the patient specifically "opts out" of HIV testing. HIV testing will be performed at the Tennessee Department of Health, Division of Laboratory Services.
3. Fill each QFT-GIT tube to the black indicator mark. Specimen amounts greater than or less than 1mm above or below the indicator mark require an immediate re-draw with a new QFT-GIT tube of the same top color. The black mark on the side of the tubes indicates the 1ml fill volume. If the level of blood in any tube is not close to the indicator line, another blood sample is to be obtained.
4. Immediately after filling tubes, invert tubes 10 times to ensure that the entire inner surface of each tube is coated with blood. It is essential that the contents of the tubes be thoroughly mixed with the blood.
 - a. Tubes should be between 17-25°C (63-77°F) at the time of filling.
 - b. Over-energetic shaking may cause gel disruption and lead to aberrant results.
5. Make sure the tubes are correctly identified to the corresponding patient.
6. **AVOID COVERING THE BLACK LINE ON THE TUBES WITH A LABEL.**
7. Place the specimen tubes upright in a rack.

Incubation

1. Incubation of the specimens must occur within 8 hours of blood collection. **DO NOT** refrigerate or freeze the blood samples.
2. Incubate the tubes upright at 37°C (98°F) ±1°C for 16-24 hours.
3. If the blood is not incubated immediately after collection, re-mixing of the tubes by inverting 10 times must be performed immediately prior to incubation.
4. Following incubation, the blood collection tubes may then be held between 4-27°C (39.2-80.6°F) for up to three (3) days prior to centrifugation at the laboratory. The tubes must be received by the Tennessee Department of Health, Division of Laboratory Services by the third (3rd) day after incubation ends.

Packaging and Shipping

- Refer to **Appendix C** QuantiFERON Policy, Laboratory Section

Documentation

- The qualitative QFT-GIT result will be indicated on the laboratory report form as **"Positive," "Negative," or "Indeterminate"**
- Document results

A negative reaction to a TST or IGRA does not exclude the diagnosis of TB infection or active TB disease.

Interferon-Gamma Release Assay (IGRA)—T-Spot.TB®

Uses

- T-Spot.TB® is a laboratory test that aids in diagnosis for both TBI and active TB disease by measuring T-cells producing interferon-gamma as a result of activation by *Mycobacterium tuberculosis* (MTB) antigens. It is one specific FDA-approved test of a general type called “interferon-gamma release assays” (IGRA)
- Single-visit, one-tube blood test for TB testing
- Does not cross-react with the BCG vaccine
- Does not cross-react with most non-tuberculosis mycobacteria
- May be used in place of (but not in addition to) a TST in all situations in which CDC recommends TB skin test as an aid in diagnosing TBI
- As with TST, live virus vaccines might affect IGRA test results. However, the effect of live virus vaccination on IGRAs has not been studied. Until additional information is available, IGRA testing in the context of live virus vaccine administration should be done as follows:
 - Either on the same day as vaccination with live-virus vaccine or 4-6 weeks after the administration of the live-virus vaccine
 - At least one month after smallpox vaccination

Reference:

1. CDC. Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection—United States, 2010. MMWR 2010; 59 (No. RR-5). <http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf>

Eligibility Requirements

- In public health clinics in Tennessee, T-Spot.TB® should only be used to test individuals who are identified through administration of the TB Risk Assessment Tool (TB RAT) as at “high-risk” for TB infection and/or the progression of TB infection to active TB disease.
- T-Spot.TB® may only be substituted for QFT-GIT on a case-by-case basis with prior approval from the TTBEPCO.
- Refer to the current TB Nursing Protocol
- Refer to the current TB Risk Assessment Tool (TB RAT) Instructions (**Appendix B**)

Exclusion Criteria

The following people are excluded from testing with T-Spot.TB®:

- Children <5 years old
- Any child, regardless of age, requiring TB testing as part of the EPSDT exam
- Any person determined to be “low-risk” through the TB RAT

- Health Care Workers (HCWs) and other individuals required by an employer or educational institution to have a baseline or serial TB test (e.g., annually) as a condition of employment or enrollment. T-Spot.*TB*® should not be used for employment/ admission testing or serial testing
- Routine testing of county jail inmates and jail employees in jurisdictions in which targeted TB testing is financially supported by the TTBEF

Specimen Collection and Handling

1. Requires whole blood.
2. Collect two (2) lithium or heparin tubes (green-top tubes). EDTA (anticoagulant gel) tubes are not recommended since they affect the secretion of interferon-gamma by the blood cells. Blood collection tubes that contain this anti-coagulant cannot be used.
3. Maintain the specimen between 18-25°C (room temperature) until processed. **DO NOT** refrigerate or freeze. Must be processed within eight (8) hours of specimen collection.
4. Store at room temperature until packaged for transport. **NOTE:** follow manufacturer’s instructions.

Labeling

The following information should be provided:

- Patient’s name
- Patient DOB
- Date and time of specimen collection
- The T-Spot.*TB*® test requisition form should be completed

Packaging

1. Insert specimen tube(s) in an absorbent tube holder. Up to six (6) patient specimens may be placed in each tube holder.
2. Place tube holders in a biohazard bag and seal. Up to two (2) tube holders may be placed in a biohazard bag.
3. Place completed requisition form(s) in the biohazard paperwork pouch.
4. Place the liquid pack in the insulated container followed by the biohazard bag containing the specimens.
5. Place the solid pack on top of the biohazard bag.
6. Close the brown flap over the solid pack and place the lid on top of the insulated container.

Shipping

1. Complete the “List of Contents” checklist printed on one of the inside flaps of the shipping box.
2. Seal the box with packaging tape and place the FedEx label on the top of the package.
3. Call for a FedEx pick-up.
4. For reference, the Oxford Diagnostic Laboratory’s T-Spot.*TB*® client services phone number is 1-877-598-2522.

Documentation

- The test result will be indicated on the laboratory report form as **“Positive,” “Negative,” “Borderline,” or “Unsatisfactory”**
- Document results

A negative reaction to a TST or IGRA does not exclude the diagnosis of TB infection or active TB disease.

5. SCREENING AND TESTING OF CONTACTS

Persons exposed to an individual with infectious TB disease are at high risk for acquiring TB infection; and, if these persons or "contacts" acquire TB infection, they are at a further risk for developing TB disease within the first two (2) years after becoming infected with TB. To prevent the development of TB disease and/or to treat the TB infection, it is important to screen and test these contacts.

- Using the concentric circle approach, organize, prioritize and screen all contacts with a TB Risk Assessment Tool which includes a symptom screening and perform a TB test according to the timeframes and priority charts found in **Module VII. Case Finding and Contact Investigation.**
- High-risk contacts must be screened and tested without delay (e.g., HIV infected or medical-risk factors and children under 5 years of age); contacts with the highest level of exposure in each of the settings are screened, tested and seen by clinician for a full medical evaluation, including a CXR.
- Medium-risk contacts are screened and tested according to the established timeframes and priority charts found in **Module VII. Case Finding and Contact Investigation.**
- Low-risk contacts are screened and tested 8-10 weeks after last known exposure to index suspect/case.
- Contacts with TB symptoms (regardless of TB test result or past-positive result) must have a medical evaluation and CXR. If there is no documentation of completed TBI treatment, they should be evaluated for treatment.
- High-risk contacts to infectious TB cases are tested for TB/HIV co-infection unless they specifically “opt-out” of HIV testing (**Standard of Public Health Practice II-3**).
- If the TB screening assessment and the TB test for a contact was negative and are done prior to 8-10 weeks from last known exposure, these contacts should be retested in 8-10 weeks from date of last TB exposure.
- For infants needing screening and testing due to recent contact to a TB case, an initial TST can be given once the child is at least three (3) months of age. Due to infants younger than six (6) months of age having an underdeveloped immune system, another TST should be given when the infant is six (6) months of age or older to rule out anergy.

Reference:

1. CDC. Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis: Recommendations from the National Tuberculosis Controllers Association and CDC. MMWR 2005; 49 (No. RR-15). <http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf>