Guidelines for Requesting Quantiferon Testing through the Connecticut Department of Public Health Laboratory

(updated March 5, 2012)

Background

Since 2001, new tests have become available to aid in the diagnosis of latent tuberculosis infection (LTBI) caused by *Mycobacterium tuberculosis* (MTB). These tests, called interferon-gamma release assays or IGRAs, detect tuberculosis antigen-induced secretion of interferon gamma by peripheral blood mononuclear cells, the immune response to MTB, but work in different ways. At the present time, three tests are FDA approved for use and commercially available: QuantiFERON® Gold (QFT-G) and QuantiFERON® Gold In-Tube (QFT-GIT) (Cellestis, Inc.) and T-SPOT.TB (Oxford Immunotec).

The advantages of IGRAs are that testing requires just a single visit for a blood draw and no patient return visit for reading the test. Since the test is performed in the laboratory, results are both objective and qualitative. The most important advantage is that these tests use components of MTB that are specific for MTB and are not shared with Bacille Calmette-Guerin (BCG) vaccines or *Mycobacterium avium intracellare* (MAI), and therefore, do not result in cross-reactivity in persons who have been vaccinated with BCG or infected with MAI. The disadvantages of IGRAs are the need for trained personnel to draw blood and the strict holding time and incubation requirements needed prior to laboratory testing of the blood specimens (1). IGRAs are also more expensive than TSTs. Some of the same issues that TSTs present in persons who are immunocompromised or taking immunosuppressant medications also exist with IGRAs since they both measure the immune response to MTB.

In 2010, the Centers for Disease Control and Prevention (CDC) released updated guidelines for using IGRAs (2). IGRAs can be used in all instances in which a TST would be used but are usually the preferred tests for patients ≥5 years old who have received BCG. It should be noted that the TST is a test with good specificity in patients who have been vaccinated with BCG and remains useful in the identification of patients with LTBI. However, it must be stated that there are a number of instances in which the IGRAs are negative while the skin tests measure greater than 15 mm induration in high-risk individuals with recent contact and without a history of BCG vaccination. There also are similar instances in which the IGRA is positive and the skin test is not. Long-term data are sparse on which test is more accurate in predicting the future development of tuberculosis disease, and although they are not equivalent tests, they still may detect a similar proportion of infected individuals (3).

Although a QFT-GIT test can be performed in lieu of the placement of a TST, at times patients may have both a TST and a QFT-GIT performed. To decrease confusion and clinical dilemmas when there is discordance between the two tests, the results of the two tests should be taken together to make clinical decisions regarding the LTBI status of patients and recommendations for treatment. A medical epidemiologist in the CTDPH TB Program is available for consultation regarding discordant test results and treatment decisions.

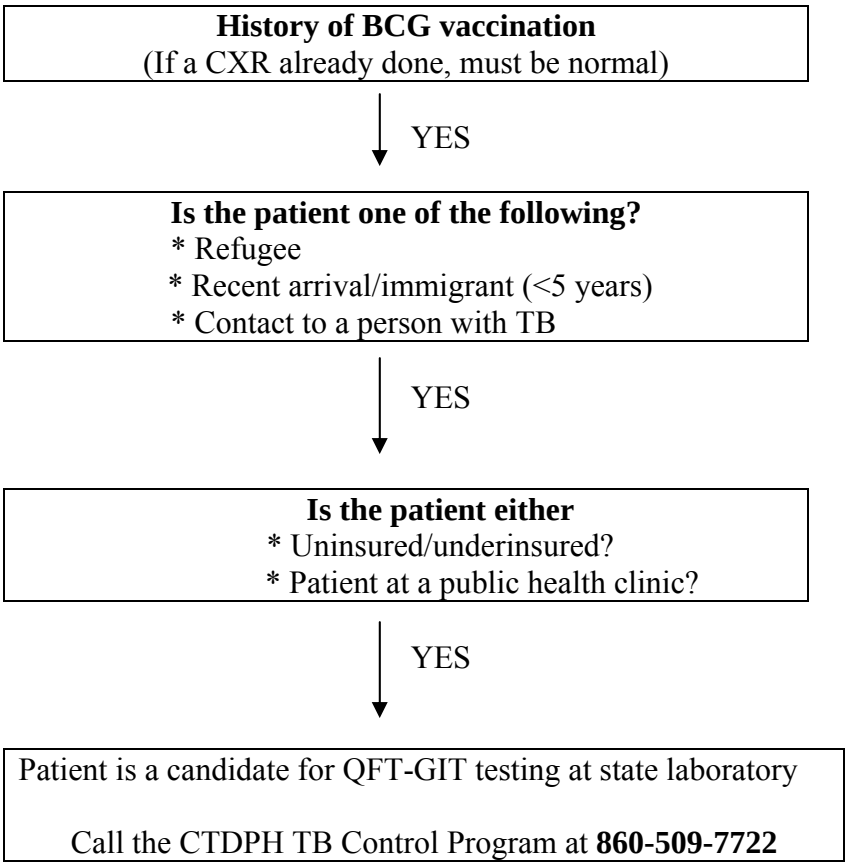
The Connecticut Department of Public Health (CTDPH) Laboratory has the capacity to perform QFT-GIT testing. This test is also offered by Quest (800-982-6810) and Clinical Laboratory Partners (800-286-9800). All requests for testing at the CTDPH Lab should first be discussed with a member of the CTDPH TB Control Program staff (860-509-7722) to determine the appropriateness of testing and to discuss testing logistics. Patients must meet the requirements below in order to request testing through the CTDPH laboratory.

How to Determine if a Patient is a Candidate for QFT-GIT Testing at the Connecticut Department of Public Health Laboratory

1. The patient must have a TB risk factor and be eligible for treatment if infected.*
The patient's TB risk assessment (and TST result if done) will be needed to make decisions regarding testing. No specimens will be tested from patients without a documented TB risk factor.

2. The intention to test is an intention to treat
Patients who are unwilling to receive treatment for LTBI are not candidates for testing at the state.

3. Algorithm for testing for QFT-GIT at the state public health laboratory



If the answer is NO to any of the questions above, request testing through a commercial lab.

* There are limited data on the use of IGRAs in certain populations including immunocompromised persons (e.g., HIV infection, immunosuppressive drugs) and young children (< 5 years old). Decisions to test specimens from these persons at the CTDPH Lab will be made on a case-by-case basis.

References

1. CDC. Updated guidelines for using interferon gamma release assays to detect *Mycobacterium tuberculosis* infection, United States—2010. MMWR 2010 59 (RR-5).
2. Quantiferon Gold In Tube Method Package Insert. Cellestis, Inc. (USA) *Doc. No. US05990301K July 2011*
3. Pai M, Zwerling A, Menzies D. Systematic Review: T-Cell-based assays for the diagnosis of latent tuberculosis infection: An update. Ann Intern Med 2008; 149: 177-184.
Cellestis Inc. (USA) Website: www.cellestis.com

QuantiFERON® TB Gold In-Tube Collection and Testing Instructions

All QFT-GIT testing at the CTDPH Laboratory **must** be pre-approved by a member of the TB Control Program (860-509-7722). The information below should be faxed to the TB Control Program (860-509-7743) for **every** test submitted.

QuantiFERON® TB Gold In-Tube Supplemental Information		
Person Requesting Test:		**Phone:**
Patient Name (Last, First, Middle)		**Date of Birth**
TST History: Date:_____	Result _____mm	☐ Not Done
BCG History: ☐ Yes	☐ No	☐ Unknown
TB Risk Factors:		
☐ Foreign-born	☐ Contact to a TB case	☐ Other, please specify: _____
☐ Homeless	☐ Illicit drug use	
☐ Corrections history	☐ Immunocompromised	

There are very strict requirements for the collection and handling of specimens for QFT-GIT testing. Please follow the below instructions below precisely to ensure the accuracy of results. Collection kits can be obtained by calling the CTDPH Laboratory at (860) 509-8501.

Specimen Collection: The test uses three specialized blood collection tubes: Nil Control Tube (Grey Cap), TB Antigen Tube (Red Cap), Mitogen Control Tube (Purple cap)

1. Using standard venipuncture technique, draw 1ml (0.8–1.2ml) of blood into each of the three specimen tubes (black mark on the side of the tube indicates the 1ml fill volume). As the tubes will fill relatively slowly, keep the tube on the needle for 2-3 seconds once the tube appears to have completed filling, to ensure that the correct volume is drawn. If a "butterfly needle " is being used to collect the blood, a "purge" tube must be used to ensure that the tubing is filled with blood prior to the QuantiFERON® TB Gold IT tubes being used. Fill the tube as close as possible to the indicator line. **Under or over-filling of the tubes outside the 0.8-1.2ml range may lead to erroneous results.**

2. Immediately after filling tubes, shake 10 times just firmly enough to ensure the entire inner surface of the tube is coated with blood. Shaking that is too vigorous could lead to gel disruption and aberrant results.

3. Label each specimen tube with the patient's name or other unique identifier and the date and time collected.

Submission Form: Complete all the required fields on the Microbiology Testing Services (OL-9B) requisition form and include as much other information as possible. SPECIMENS WILL NOT BE TESTED WITHOUT THE DATE AND TIME OF COLLECTION NOTED ON THE FORM. Check the box the box labeled 129M, Quantiferon–TB Test.

Packaging and Shipping:

1. Package the specimens and paperwork using the shipping supplies provided.

2. **Transport specimens** to the Conn. Dept. of Public Health (CTDPH) Laboratory **AS SOON AS POSSIBLE**. Always maintain tubes at room temperature (17°C - 27°C) prior to and during transport to the laboratory. **DO NOT refrigerate. Do NOT centrifuge.**

PLEASE NOTE: The CTDPH Laboratory will only accept specimens for testing Monday through Friday, 8:00 AM–2:00 PM. **SPECIMENS MUST BE RECEIVED AT THE LABORATORY NO LATER THAN 2:00 PM AND WITHIN 14 HOURS OF COLLECTION.**

Contact Information: For testing information and to order collection tubes, shipping supplies and requisitions: contact the CTDPH Laboratory Serology Laboratory Ph: (860) 509-8567; Fax: (860) 509-8659