City and County of San Francisco

Department of Public Health

Tuberculosis Control Section

L. Masae Kawamura, MD Director

San Francisco Guidelines on the Use of QuantiFERON-TB Gold (In Tube Method) for the Diagnosis of Latent TB Infection

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The TB Control Section of the San Francisco Department of Public Health strongly advocates the use of QuantiFERON®-TB Gold (In Tube Method) (QFT) as a diagnostic aid for determination of latent TB infection (LTBI) in accordance with the guidelines written below, and encourages laboratories to make this test available to providers.

Rationale

- Operational limitations of the TST are well known by practitioners. Two patient visits are required to obtain a reading, taking up considerable resources for both patients and providers, and resulting in many unread TSTs. There is well-documented inter-reader variability in measuring the size of a skin test even among trained health care providers. Patient factors such as prior BCG vaccination, infection with non-TB mycobacteria, and immunosuppression may result in false positive and false negative readings. The TST can boost past sensitization to mycobacterial antigens leading to complex serial testing recommendations. All of these factors make the TST a frustrating test for patients and providers and have led to recommendations that are often poorly understood, accepted, or followed.
- The QFT addresses many of the limitations of the TST. Only one-visit is required to draw blood and the laboratory test results are objective and reproducible. QFT tests multiple antigens simultaneously and does not boost amnestic immune responses (Pai et al. Lancet Infect Dis 2004; 4:761-76). Moreover, as compared to the TST, QFT appears to more reliably distinguish between BCG and TB sensitization. Limitations of QFT include the need for phlebotomy, lack of laboratories that process the test, and lack of institutional experience with interpreting this new test. A current health systems cost analysis of QFT use in San Francisco shows that QFT is cost saving compared the TST. The specificity of QFT has drastically reduced positive rates by 60-70% resulting on significant savings from unneeded chest x-rays, medical evaluation and treatment.
- National guidelines for QFT-Gold® (In Tube Method) and other IGRAs are being finalized this year. IGRAs can be used in place of the TST and are preferred in BCG vaccinated individuals and populations with low return rates for TST. Caution is advised when interpreting the negative results in children under 5 because of lack of adequate studies in this risk group. Until more studies are available, TST will be considered the preferred test in children less than 5 years of age.

When to Screen for TB

TB testing is recommended for the following groups:

- Contacts of persons with pulmonary or laryngeal TB disease
- Foreign-born persons born in countries outside of the U.S. (excluding Canada, Western Europe, Australia and Japan)
- Marginally housed or homeless persons
- Persons with prolonged (>1 month) or frequent travel (≥ twice/year) to TB–endemic countries

- Employees or residents of congregate settings, such as hospitals, dialysis units, correctional facilities, homeless shelters, nursing homes, single-room occupancy hotels, or substance abuse treatment centers
- Persons with medical risk factors for TB disease progression, such as:
  - HIV infection
  - Diabetes mellitus (prioritize screening foreign-born and homeless)
  - Prolonged corticosteroid therapy or other immunosuppressive therapy (such as TNF-antagonists, post-transplant immunosuppressive drugs, cancer chemotherapy, etc.)
  - Persons with radiographic evidence of previous TB
  - Current and former tobacco smokers (prioritize screening foreign-born and homeless)
  - Cancer of the head and neck, hematologic malignancy (e.g., leukemia and Hodgkin's disease)
  - End-stage renal disease
  - Organ transplant candidates/recipients
  - Intestinal bypass or gastrectomy, chronic malabsorption syndromes
  - Low body weight (10% or more below ideal)
  - Silicosis

Choosing the Right TB Test

- In general, patients should receive a Quantiferon test (QFT) *unless*:
  - Phlebotomy is refused
  - Phlebotomy is impractical (e.g., no veins, very young child)
  - The specimens cannot be transported to the SFDPH laboratory before 4:30 PM Monday–Friday, and the patient cannot return for phlebotomy during the specified hours
  - QFT test is not routinely available
- If patient refuses test:
  - Patient may opt for the TB skin test (TST) instead and will need to return to clinic in 48–72 hours following placement for the skin test reading.
- For special circumstances *additional tests are needed to maximize the sensitivity of diagnosing LTBI*:
  - TB suspects (ATS class "TB 5") with no prior testing or past negative TB test results:
    - Use <u>both</u> the TST and QFT to increase sensitivity (may be done on the same day)
    - Collect 3 sputum for AFB examination and culture
    - Obtain a chest x-ray (CXR) if most recent film was taken prior to symptom development or is older than 3 months
  - Asymptomatic patients who are TB test negative and on immunosuppressive therapy:

  - Use QFT or TST as a second test
  - Obtain a chest x-ray
- Immunosuppressive agents likely to cause false negative results include prednisone, methotrexate, post-transplant immunosuppressive medications and other cancer chemotherapeutic agents
- The chest-xray shall serve as a third diagnostic to look for evidence of TB infection (granuloma, hilar calcification, apical pleural thickening, upper lobe volume loss, fibrotic infiltrate(s), etc.)

Patient Registration

- To get a blood test, patients need a Community Health Network (CHN) medical record number (also known as a "B-number"). Routine patient registration should now include assignment of a "B-number" to all clients who will be tested or medically evaluated for TB. This procedure will facilitate clinic administration and laboratory results record keeping.

Pre-Test Counseling

- Major points to let patients know:
  - New blood test to assess TB infection instead of old skin test.
  - We'll draw three small tubes of blood.
  - No other blood tests will be conducted on that specimen other than the QFT

Specimen Collection and Handling

- Standard SF DPH laboratory test request forms are to be used. When completing the standard form, under the "TB tests" section check off the "other – QFT" box. Be sure to indicate which clinic/health center you are sending the result from. **If the patient has Medi-Cal, enter the medical number on the appropriate line of the laboratory request form.**
- Blood should be drawn by nurses or clinic staff certified as phlebotomists. Patients may sometimes react adversely to blood draws. Make sure to let the patient sit for a moment after blood draw, offer a cup of water, and if they appear unwell alert the clinic RN to assess and assist the patient.
- Specimens will be handled in accordance with SFGH infection control policies. To optimize blood collection into the tubes if using a butterfly needle, allow the tubing to completely fill with blood prior to filling the specimen tubes (a purge tube can be used although our staff have not found it necessary). A minimum of 1 cc blood is to be drawn into three QuantiFERON®–TB Gold In Tube (IT) blood collection tubes. After blood draw, immediately **shake the tubes vigorously for 5 seconds and label** each tube by placing the label upright and folded in half around the very top of the tube, creating the effect of a flag. Place tubes in the test tube rack with lab request form. Record the blood draw in the clinic laboratory logbook (e.g. the blue book in WD94). Specimens must be incubated within 16 hours of blood draw, hence assure delivery to the SFDPH laboratory by 4:00 pm, M-F. If incubating on-site, place the specimen rack into the incubator at

37ºC at ~4:30 pm, after a repeat vigorous 5-second shake (the whole rack can be shaken between 2 pieces of cardboard. Log in the date and time. The following day, remove specimens from incubator at 11am and place them in the designated specimen container at room temperature (2-26–C) for delivery to the DPH laboratory.

- The designated specimen container is to be delivered to the DPH laboratory (101 Grove) by 4:00 PM, **Monday through Friday** via the routine TB laboratory courier. On Fridays, two containers of specimens will be delivered: the specimens stored for transport at room temperature, and specimens drawn that day (Friday), which need to be kept in the portable incubator at 37ºC.

Patient Follow-up Instructions

- After the blood draw:
  - Advise the patient to return in three (3) working days for results
  - Give the patient an appointment card

Chart Recording and Documentation

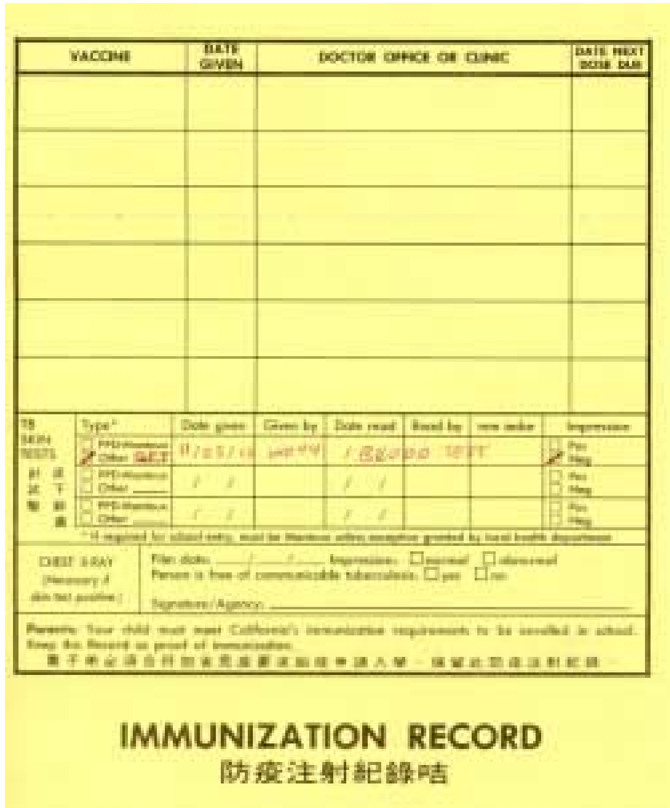
- For patients who have a blood specimen taken for QFT, flag the chart for laboratory test follow-up. Results are to be reviewed as they would be for any blood test. At the end of the next day, or the following morning, the responsible RN or HCW will lookup the patient test result on INVISION/LCR, print out a paper copy of the results for the patient chart, and interpret and act on the results.

Result Interpretation and Action Plan

- If the result is:
  - **Positive**: Interpret same as if TST positive – TB47 referral to WD94, CXR, medical evaluation *or* per MD orders
  - **Negative**: Interpret same as if TST negative – e.g. close chart & give clearance card *or* per MD orders
  - **Indeterminate**: Test failure – cannot be interpreted. Repeat QFT or if difficult blood draw, TST indicated

Communication of Results

- The same procedures used for TST/PPD results will be used. Results will be given back to patients at their return visit. To give results back to patients, the standard immunization card may be used, with slight modifications as shown below. Under type of test, mark “Other – QFT”, date given, clinic, and note “blood test”.



VACCINE	DATE GIVEN	DOCTOR OFFICE OR CLINIC	DATE NEXT DOSE DUE

TB SKIN TESTS	Type*	Date given	Given by	Date read	Read by		Impression

CHEST X-RAY

Signature/Agency:

IMMUNIZATION RECORD

防疫注射紀錄咭

- If a patient with a *negative* QFT does not return to pick up their test results, the chart can be closed. If a patient with a *positive* QFT does not return to pick up their test results, actions are the same as if a referred TST/PPD positive patient did not come to WD94 for CXR and medical evaluation. This means follow-up of the TB47 (TOPS/CHOPS) or blood test (WD94) with reminder cards (3) and phone calls (3).