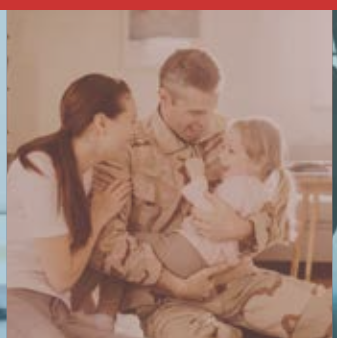
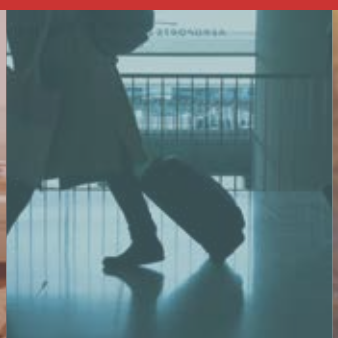
BioReference
LABORATORIES
an OPKO Health Company

QuantiFERON®-TB Gold

ERADICATING TUBERCULOSIS THROUGH PROPER DIAGNOSIS AND DISEASE PREVENTION

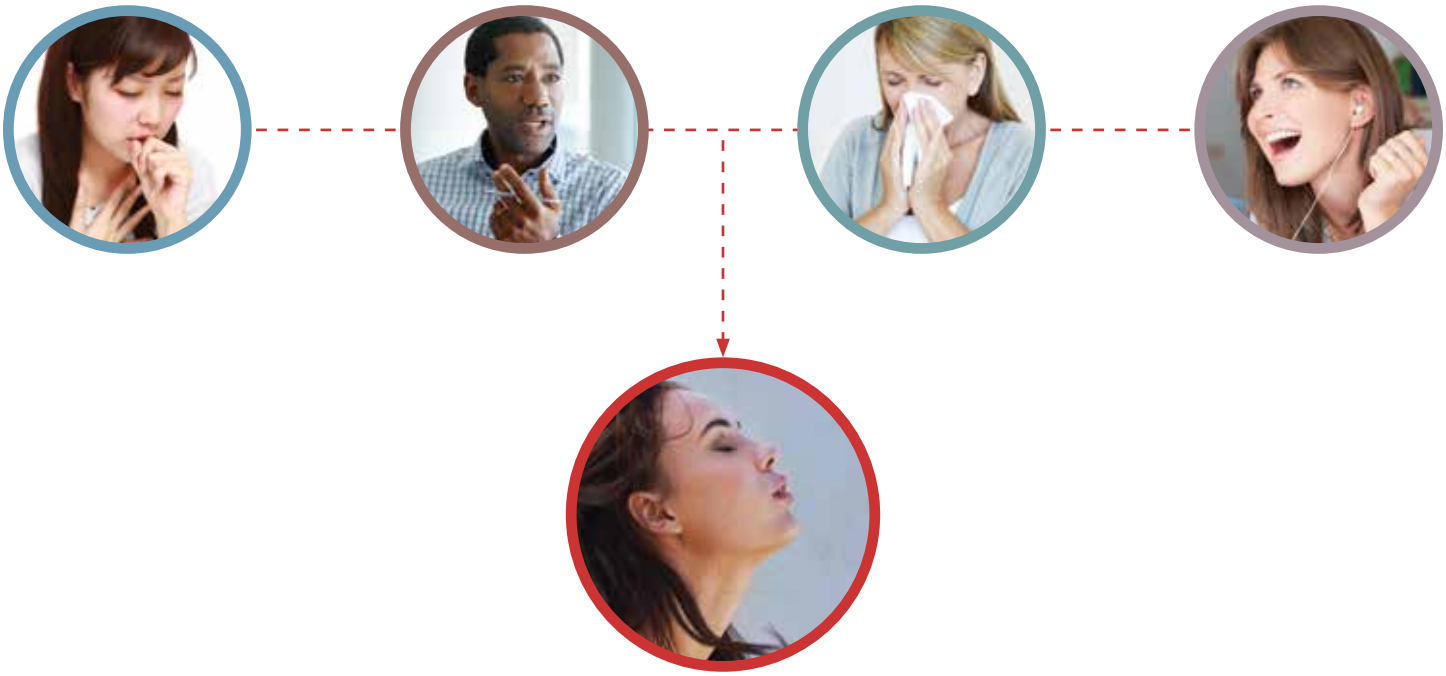




TUBERCULOSIS

Tuberculosis (TB) is caused by exposure to Mycobacterium tuberculosis (M. tuberculosis), which is spread through the air from one person to another. At least two billion people are thought to be infected with TB and it is one of the top 10 causes of death worldwide. To fight TB effectively and prevent future disease, accurate detection and treatment of Latent Tuberculosis Infection (LTBI) and Active TB disease are vital.

TRANSMISSION

M. tuberculosis is put into the air when an infected person coughs, speaks, sneezes, spits or sings. People within close proximity may inhale these bacteria and become infected. M. tuberculosis usually grows in the lungs, and can attack any part of the body, such as the brain, kidney and spine.



SYMPTOMS

People with LTBI have no symptoms. People with TB disease show symptoms depending on the infected area of the body. TB disease in the lungs may cause symptoms such as:

- A cough lasting 3 weeks or longer
- Coughing up blood or sputum
- Chest pain

Other symptoms can include:

- Chills
- Fatigue
- Fever
- Weight loss and/or loss of appetite
- Night sweats

SCREENING

To reduce disparities related to TB, screening, prevention and control efforts should be targeted to the populations at greatest risk, including:

- HEALTHCARE WORKERS
- MILITARY PERSONNEL
- ELDERLY PEOPLE
- STUDENTS
- IMMIGRANTS
- INTERNATIONAL TRAVELERS
- RESIDENTS OF LONG-TERM CARE FACILITIES
- PEOPLE WITH WEAKENED IMMUNE SYSTEMS
- PERSONS LIVING IN CORRECTIONAL FACILITIES OR OTHER CONGREGATE SETTINGS
- CLOSE CONTACTS OF PERSONS KNOWN OR SUSPECTED TO HAVE ACTIVE TB

BIOCHEMISTRY

T-lymphocytes of individuals infected with M. tuberculosis secrete interferon-gamma (IFN-γ) when they are exposed to specific antigens displayed by M. tuberculosis. The tuberculosis screen measures the IFN-γ levels in a whole blood specimen using a very sensitive interferon-gamma release assay (IGRA). Specifically, the diagnostic test detects cell-mediated immune response to two proteins that are made by M. tuberculosis, but that are absent from most other related mycobacteria species with the exception of M. kansasii, M. szulgai and M. marinum. In addition, the proteins are absent from patients that have received the Bacillus Calmette-Guerin (BCG) vaccine.

NEW PARADIGM **IN DIAGNOSING TB**

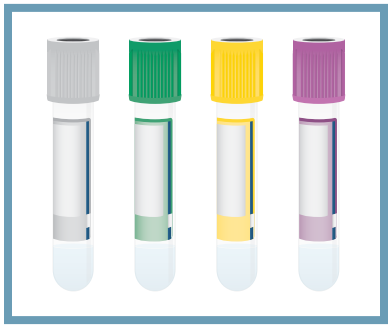
QuantiFERON-TB Gold® (QFT) is a highly specific, controlled diagnostic blood test for detecting exposure to M. tuberculosis using whole blood specimen. QFT provides the value of a robust technology, and offers physicians a more reliable and convenient tool for accurately identifying M. tuberculosis complex, which includes M. tuberculosis, M. africanum and M. bovis.

QTF is able to measure the levels of IFN-γ and correlate those levels to the presence or absence of TB disease. When compared with other IGRA products, which require subjective counting of spots, QFT provides quantitative detection with a user-friendly workflow.

TEST INFORMATION	QUANTIFERON RESULTS
Performance specifications	Sensitivity – >94% Specificity – >97%
Sample input	Incubated whole blood
Blood draw dependent on age or immune status?	No
Measurement	Detection of IFN-γ by optical density measurement
Objective result	Yes
Perfomance in immunosuppressed populations	Proven performance in patients who are taking immune suppression therapies (methotrexate, corticosteroids and TNF-inhibitors)
Reproducibility	Inter-assay variability – 8.7% Intra-assay variability – 6.6% Inter-observer variability – not applicable

TEST ADMINISTRATION AND PROCEDURE

QFT has unique blood collection tubes, enabling immediate exposure of blood lymphocytes to highly specific TB antigens and test controls coated on the inner surface of the tubes. The Nil tube (negative control) adjusts for background IFN-γ. The Mitogen tube serves as a positive control and can be useful for indicating correct sample handling and incubation, as well as a patient's immune status. The TB1 and TB2 Antigen tubes provide a more comprehensive view of the immune response to a TB infection through use of CD4/CD8 technology.



Blood is collected by venipuncture for testing. Evacuated tubes should be filled to the 1 mL line with blood, handled at room temperature and TRANSPORTED TO THE LABORATORY FOR TESTING WITHIN 16 HOURS OF COLLECTION. ***Blood samples are incubated with the test antigens. After incubation, the concentration of IFN-γ is determined in the samples by ELISA, using the reagents in the test kit.***

ADVANTAGES OVER **TRADITIONAL TUBERCULIN SKIN TEST**

QFT can aid in the diagnosis of both active TB disease and LTBI. It is applicable to all patient groups who would be candidates for the traditional tuberculin skin test, but has several significant advantages:

- **ACCURACY** – QFT is a blood test that assesses the production of gamma interferon by a type of white blood cell, and is a sensitive test for exposure to TB. A positive result means that the patient has been exposed to the M. tuberculosis bacterium, which may be either latent (asymptomatic) or active. Most results of the test (>95%) result in either a positive or negative result, and is not affected by compromised immunity, such as may seen in HIV patients.
- **CONVENIENCE** – Can generate the desired disease information after a single patient visit, whereas a TB skin test must be evaluated by a clinician in a subsequent visit days after the test.
- **RELIABILITY** – The TB skin test requires an intradermal injection which is subject to health provider error in administration. It also requires a second visit to the health care provider after 2-3 days to interpret the test. False positives with the skin test may occur in the setting of BCG (Bacillus Calmette-Guerin) vaccination/administration, and false negatives may occur in immunocompromised patients.

THE US CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) GUIDELINES RECOMMEND THE USE OF AN INTERFERON-GAMMA RELEASE ASSAY (IGRA) IN ALL SITUATIONS IN WHICH THE TB SKIN TEST WAS TRADITIONALLY USED, WITH IGRAS BEING THE PREFERRED TEST FOR PERSONS WHO HAVE BEEN BCG – VACCINATED OR ARE UNLIKELY TO RETURN FOR TB SKIN TEST READINGS.

TEST INFORMATION

TEST CODE: T814-3
METHODOLOGY: Enzyme-Linked Immunosorbent Assay (ELISA)
COLLECTED: Please direct patients to their nearest patient service center for specimen collection. Specimens should arrive in the laboratory no later than 4pm.
PERFORMED: Monday – Sunday
REPORTED: 24 – 48 hours
SPECIMEN REQUIREMENTS: **1.** Collect 1 mL of blood into Nil, TB1, TB2 and Mitogen tubes (fill to blank line). Note: If butterfly needle is used, a purge tube must be collected first. **2.** Mix well for five seconds (10 times) at room temperature. **3.** Label tubes and shipper with patient name, account number, date collected, time collected and phelbotomist name. **4.** Ship to lab at room temperature.
PROCESSING: Submit original collection device with requisition.
STORAGE: Please store sample at room temperature.
UNACCEPTABLE CONDITIONS: Hemolyzed, frozen or refrigerated blood is not acceptable and will be rejected for testing. Specimens received 16 hours after draw will be rejected for testing.

REFERENCES

1. Thomas R. Frieden, MD, MPH, Bureau of TB Control, QFT-G Provider Fact Sheet, February 2007.
2. Geral`d H. Mazurek, MD, John Jereb, MD, Phillip LoBue, MD, Michael F. Iademarco, MD, Beverly Metchock, PhD, Andrew Vernon, MD, Guidelines for Using the QuantiFERON®-TB Gold Test for Detecting Mycobacterium tuberculosis Infection, United States, December 16, 2005 / 54(RR15);49-55.
3. Cellestis Clinicians Guide to QuantiFERON®-TB, Gold Clinicians Guide 05981000A, January 13th, 2005, 90912 11/15.
4. Abu-Raddad, L.J., et al. Epidemiological benefits of more-effective tuberculosis vaccines, drugs, and diagnostics. Proc. Natl. Acad. Sci., USA 106,13980.
5. World Health Organization (2013). Global tuberculosis report 2013. www.who.int.tb/publications/global_report/en
6. Centers for Disease Control and Prevention (2010). Updated guidelines for using interferon-gamma release assays to detect Mycobacterium tuberculosis infection – United States. MMWR 59(RR05), 1.
7. QuantiFERON-TB Gold Package Insert. March 2013. US05990301L. US customers should consult current online version for their country at www.QuantiFERON.com
8. Baussano, I., Nunn, P., Williams, B., Pivetta, E., Bugiani, M., and Scano, F. (2011). Tuberculosis among health care workers. Emerg. Infect. Dis. 17, 488.
9. Cheallaigh, C.N., et al. (2013). Interferon gamma release assays for the diagnosis of latent TB infection in HIV-infected individuals in a low TB burden country. PLoS One 8, e53330.
10. Hoffmann, M., Tsinalis, D., Vernazza, P., Fierz, W., and Binet, I. (2010). Assessment of an interferon-gamma release assay for the diagnosis of latent tuberculosis infection in haemodialysis patients. Swiss Med.Wkly. 140, 286.
11. Kwakernaak, A.J., Houtman, P.M.,Weel, J.F., Spoorenberg, J.P., and Jansen, T.L. (2011). A comparison of an interferon-gamma release assay and tuberculin skin test in refractory inflammatory disease patients screened for latent tuberculosis prior to the initiation of the first tumor necrosis factor a-inhibitor. Clin. Rheumatol. 30, 505.
12. Pratt, A., Nicholl, K., and Kay, L. (2007). Use of the QuantiFERON TB Gold test as part of a screening programme in patients with RA under consideration for treatment with anti-TNF-a agents: The Newcastle (UK) experience. Rheumatology (Oxford) 46, 1035.
13. Diel, R., Loddenkemper, R., and Nienhaus, A. (2010). Evidence-based comparison of commercial interferon-gamma assays for detecting active TB: a metaanalysis. Chest 137, 952.
14. Harada, N. et al. (2008). Comparison of the sensitivity and specificity of two whole blood interferon-gamma release assays for M. tuberculosis infection. J. Infect. 56, 348.
15. T-SPOT®.TB Package Insert. Oxford Immunotec Inc. 2013. PI-TT.610-US-V4.

QuantiFERON®-TB Gold (QFT®) is CE marked. QFT is approved by the US FDA. QFT Package Inserts, available in multiple languages, as well as up-to-date licensing information and product specific disclaimers can be found at www.QuantiFERON.com

BioReference LABORATORIES
an OPKO Health Company

481 Edward H Ross Drive ▪ Elmwood Park, NJ 07407 ▪ 1-800-229-5227 tel ▪ 1-201-791-1941 fax ▪ www.BioReference.com