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CHANGES TO QUANTIFERON-TB GOLD PLUS

On June 23, 2021, TriCore Reference Laboratories will change the reporting of QuantiFERON-TB Gold Plus test results. Per CDC guidelines, results will now be qualitatively and quantitatively reported.[1] These data may help with interpretation of the test results.

What is the QuantiFERON-TB Gold Plus test?

QuantiFERON-TB Gold Plus (QFT-Plus) is an interferon-gamma release assay which is an indirect test for *Mycobacterium tuberculosis* (TB) infection. It should be used in conjunction with clinical assessment, radiography, and potentially other tests to assess for **exposure** to *M. tuberculosis*. Detection of interferon-gamma is used to identify *in vitro* responses to peptide antigens that are associated with latent or active *M. tuberculosis* infection. More information about interferon-gamma release assays is available from the CDC.[2]

Interferon-gamma is measured in blood samples collected into four tubes:

1. The Nil tube: This tube detects nonspecific interferon-gamma release from T-cells.
2. The Mitogen tube: This tube detects the ability of T-cells to release interferon-gamma.
3. The TB1 tube: This tube detects if T-cells release interferon-gamma in response to specific *M. tuberculosis* antigens (ESAT-6 and CFP-10) from CD4+ helper T-cells. This may indicate that T-cells have seen these antigens before and may suggest prior exposure to *M. tuberculosis*.
4. The TB2 tube. This tube detects if T-cells release interferon-gamma in response to an additional set of *M. tuberculosis* antigens targeted to stimulate responses from CD8+ cytotoxic T-cells. This may indicate that T-cells have seen these antigens before and may suggest prior exposure to *M. tuberculosis*.

How is the reporting of QFT-Plus test results changing?

Results will continue to be reported qualitatively as nonreactive, indeterminate, or reactive along with an interpretive comment. Now quantitative results of interferon-gamma will also be available and reported as follows:

- NIL
- TB1 minus NIL
- TB2 minus NIL
- Mitogen minus NIL

Most clinicians should continue to use the qualitative results for interpreting QFT-Plus test results. Additional details about the significance of the different values generated by the QFT-Plus test have been described.[1]

Can QFT-Plus distinguish between active TB and latent TB infection?

Current evidence suggests that higher CD8+ activity may occur in individuals with active TB; however, there is insufficient evidence to state that QFT-Plus can distinguish between active TB and latent TB infection. *Therefore, QFT-Plus should never be used in isolation to diagnose an individual with active TB or latent TB infection.* Anyone with a reactive QFT-Plus test result should be assessed for active TB infection with a clinical evaluation including an assessment for prior exposure to *M. tuberculosis*, current symptoms, a chest radiograph and potentially other relevant tests. For further assistance, please reach out to the New Mexico Department of Health Tuberculosis Prevention Program.[3]

Can QFT-Plus be used for children and other specific populations?

Published data indicates that QFT-Plus performs as well in children as it does in adults and there is no apparent loss of performance in children under 5 years. However, the performance of the QFT-Plus test has not been extensively evaluated in individuals younger than 17 years of age, immunocompromised patients, or pregnant women. QFT-Plus is the preferred test in individuals with a history of Bacille Calmette-Guérin (BCG) vaccination, a vaccine commonly given to individuals in countries with high incidence of TB. Unlike the TB skin test, QFT-Plus can distinguish actual TB infection from BCG vaccination history. More information about the BCG vaccine is available from the CDC.[4]

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[1] Mazurek GH, et al. Updated guidelines for using Interferon Gamma Release Assays to detect *Mycobacterium tuberculosis* infection - United States, 2010. MMWR 2010;59:1-25 (https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5905a1.htm)

[2] Interferon-Gamma Release Assays (IGRAs) – Blood Tests for TB Infection (https://www.cdc.gov/tb/publications/factsheets/testing/igra.htm)

[3] NMDOH Tuberculosis Prevention Program (https://www.nmhealth.org/about/phd/idb/tbpp/)

[4] BCG Vaccine (https://www.cdc.gov/tb/publications/factsheets/prevention/bcg.htm)

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CHANGES TO QUANTIFERON-TB GOLD PLUS, CONTINUED

QuantiFERON TB Gold Plus		
Test Code: TBGPLS	Testing Performed: Monday-Friday	Reported: Within 1-3 days
CPT Code: 86480	Methodology: Immunoassay	
COLLECTION/PROCESSING (altitudes lower than 6,150 feet)		
Specimen	Whole Blood	
Collection Containers	4 Tube QFT-Plus Collection Tubes	
Collection Amount	Collection tubes are designed to collect 0.8 - 1.2 mL of whole blood. The black line on each tube indicates 1.0 mL fill line.	
Instructions	Tube temperature should be between 17 and 25 degrees Celsius (63 and 77 degrees Fahrenheit) at the time of blood tube filling. All 4 tubes must be collected. The order of collection is not critical. The tubes draw blood slowly. Keep the tube on the needle for 2 to 3 seconds once the tube appears to have completed filling. This will ensure that the correct volume is drawn. NOTE: if a butterfly needle is being used to collect blood, a “purge” tube should be used to ensure that the tubing is filled with blood prior to the QFT-Plus Blood Collection Tubes being used. The black mark on the side of the tubes indicates the validated range of 0.8 to 1.2 mL. If the level of blood in any tube is outside of the indicator mark, a new blood sample should be obtained. Under- or over-filling of the tubes outside of the 0.8 to 1.2 mL range may lead to erroneous results. Immediately after filling tubes, shake them ten (10) times just firmly enough to ensure the entire inner surface of the tube is coated with blood, to dissolve antigens on tube wall. CAUTION: overly vigorous shaking may cause gel disruption and could lead to aberrant results. Label tubes appropriately. DO NOT centrifuge, refrigerate, or freeze the specimens.	

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CHANGES TO QUANTIFERON-TB GOLD PLUS, CONTINUED

QuantiFERON TB Gold Plus, continued	
COLLECTION/PROCESSING (altitudes higher than 6,150 feet)	
Specimen	Whole Blood
Collection Containers	Lithium Heparin (Green-top) Tube AND 4 Tube QFT-Plus Collection Tubes
Collection Amount	5 mL (minimum)
Instructions	Label single blood collection lithium heparin tube and QFT-Plus Blood Collection Tubes, 4-tube set, appropriately. Tube temperatures should be between 17 and 25 degrees Celsius (63 and 77 degrees Fahrenheit) at the time of blood tube filling. Collect minimum 5 mL of blood by venipuncture directly into the single lithium heparin tube. Gently mix by inverting the tube several times to dissolve the heparin. Dispense exactly 1 mL of blood to each of the four QFT-Plus Blood Collection Tubes. All 4 tubes must be filled with 1 mL of blood. Under- or over-filling of the tubes may lead to erroneous results. The order of filling is not critical. Immediately after filling tubes, shake them ten (10) times just firmly enough to ensure the entire inner surface of the tube is coated with blood, to dissolve antigens on tube wall. CAUTION: overly vigorous shaking may cause gel disruption and could lead to aberrant results. Label tubes appropriately. DO NOT centrifuge, refrigerate, or freeze the specimens.
SHIPPING/TRANSPORT AND STORAGE	
Shipping Instructions	Transport at ambient temperature. Samples must arrive at TriCore's core laboratory in Albuquerque within 12 hours of collection.
Stability/Storage: (*collection to initiation of testing*)	Ambient: 12 hours Refrigerated: Unacceptable Frozen: Unacceptable

A video showing proper collection and shaking of the QFT-Plus Blood Collection tubes can be found here:

https://vimeopro.com/tricore/tbgold