

1. The evaluation of the QFT in populations with very low prevalence and with individuals with confirmed tuberculosis should be a surrogate for inferring sensitivity and specificity of the QFT. However, literature evidence indicates depression of IFN- γ production with active tuberculosis. Thus, QFT results in these patients cannot be used as a marker for ability to detect latent infection.

How would you interpret TST+/QFT- and TST-/QFT+ findings in the data provided to support QFT performance? In other words, would you consider:

- a. Positive QFT results in the low risk populations to likely be true cases of latent TB that were missed by TST, or would you consider these positive QFT results likely to be falsely positive?
- b. Negative QFT results to likely be evidence of no latent TB infection in subjects whose TST is positive?

2. Taking into consideration the points below, how can the data available be used to evaluate individual patients and their probability for latent TB infection when the QuantiFERON-TB assay is positive or negative for individuals:

- a. who have had close contact with an infected individual?
- b. from an area where tuberculosis is prevalent?
- c. with potential occupational exposure?
- d. with no known risk factors? or
- e. with prior BCG vaccination?

3. Given differences in QFT results that would be seen using different cutoffs, particularly for the low risk groups, how could the labeling provide directions for interpreting QFT results and describe performance? What contraindications, warnings or limitations on the use of the product might be appropriate?