

# QFT-Plus FAQ

## 1. How does the QFT-Plus assay differ from the QFT In-Tube assay?

The QFT-Plus will provide similar information as the QFT In-Tube assay, and includes a second TB antigen tube that allows the measurement of interferon gamma released by CD8+ T cells as well as CD4+ T cells. The addition of the second TB antigen tube has been included to increase the sensitivity of the assay to detect TB, particularly in immunosuppressed populations.

## 2. How will the collection of blood samples differ for the QFT-Plus assay compared with the QFT In-Tube assay?

The phlebotomy practice and handling process will be the same as the QFT In-Tube with the exception of an additional tube that contains TB antigens that stimulate interferon gamma release by CD4+ and CD8+ T cells.

## 3. How do the tubes differ in the QFT In-Tube assay from the QFT-Plus assay?

The nil and mitogen tubes from the QFT In-Tube assay are essentially the same in the QFT-Plus assay. The TB antigen tube from the QFT In-Tube assay is called “TB1” in the QFT-Plus assay and measures the interferon gamma released by CD4+ cells when exposed to TB antigens ESAT-6 and CFP-10. In the QFT-Plus assay, TB1 does not include one of the TB antigens included in the QFT In-Tube assay, which is Protein 7.7. Also, an additional TB antigen tube is included in the QFT-Plus assay. The new TB antigen tube in the QFT-Plus assay is called “TB2” and measures the interferon gamma released by both CD4+ and CD8+ T cells when exposed to TB antigens, which are short peptides derived from CFP-10. The loss of Protein 7.7 from the QFT In-Tube assay reduces the sensitivity of TB1, but the addition of TB2 preserves and is thought to enhance the overall sensitivity of QFT-Plus relative to QFT In-Tube.

## 4. How is the QFT-Plus assay interpreted?

Positive results by TB1, TB2, or both are considered positive. See the table below.<sup>1</sup>

Interpretation of QFT-Plus results					
Nil	TB1 minus Nil (IU/ml)	TB2 minus Nil (IU/ml)	Mitogen minus Nil (IU/ml)	QFT-Plus result	Report/Interpretation
< 8.0	≥0.35 and ≥25% of Nil	Any	Any	Positive	M. tuberculosis infection likely
	Any	<0.35 or ≥0.35 and <25% of Nil			
	<0.35 OR ≥0.35 and <25% of Nil		≥0.5	Negative	M. tuberculosis infection NOT likely
			<0.5	Indeterminate	Likelihood of M. tuberculosis infection cannot be determined
≥8.0	Any				

## 5. Can the QFT-Plus differentiate between active TB disease and TB infection?

Current evidence may suggest higher CD8 activity in active TB, however, there is insufficient evidence to indicate that QFT-Plus can distinguish between active TB and TB infection. Therefore, QFT-Plus should never be used in isolation to diagnose active TB or TB infection. Anyone testing positive should be assessed for active TB with a medical evaluation, chest radiograph and other tests indicated by the clinical symptoms and medical evaluation.

## 6. What is the sensitivity and specificity of the QFT In-Tube and QFT-Plus for TB infection?

In peer reviewed reports, the reported sensitivity of the QFT In-Tube and QFT-Plus assays for TB infection were 84%-94% and 83-91%, respectively, and the specificity of the QFT In-Tube and QFT-Plus assays for TB infection were 99% and 97%-98%, respectively.<sup>2,3</sup>

**7. How often does QFT-Plus yield an indeterminate result?**

QFT-Plus indeterminate results generally occur very infrequently in healthy individuals. In clinical studies for QFT-Plus, the indeterminate rate was less than 2.5% for active TB. However, in populations where the level of immunosuppression is high, past studies of QFT show that indeterminate rates can be correspondingly higher.<sup>1</sup>

**8. What should I do if the QFT-Plus result is indeterminate?**

When presented with an indeterminate result, physicians may choose to redraw a specimen or perform other procedures, as appropriate. However, an indeterminate QFT-Plus is meaningful, suggesting possible error in performing the test or immunosuppression – particularly in patients with known or suspected immunosuppression, chronic disease, malnutrition or on medications known to decrease immunity.<sup>1</sup>

**9. Why would I see false-negative results in patients with active TB?**

Individuals who progress to active TB do so because their immune system cannot control their infection. This can result from a large infectious exposure to *M. tuberculosis*. It may also be due to individuals having an impaired immune response, typical for malnourished individuals, those with advanced TB, those who are severely immunosuppressed or whose immune function has altered. Some individuals may develop active TB as a result of a genetic deficiency in their immune system, such as an inability to produce sufficient IFN- $\gamma$  and/or IL-12. Others may develop active TB as a result of iatrogenic immune suppression, for example, individuals taking anti-TNF- $\alpha$  medications. It is important to note that QFT-Plus is a test for *M. tuberculosis* infection and is approved as a diagnostic aid for indirect detection of *M. tuberculosis* infection (whether active TB disease or TB infection). Clinicians may use QFT-Plus to assist in the diagnosis of active TB (in conjunction with risk assessment, radiography and other medical and diagnostic evaluations). A negative QFT-Plus result in a person with obvious symptoms of active TB should by no means be used to rule out active disease. Culture of *M. tuberculosis* remains the gold standard for confirming a diagnosis of active TB.

**10. When will the QFT-Plus assay be available for use in patients in the U.S.?**

The QFT-Plus assay was released in October 2017. LA County Public Health Laboratory will be targeting implementation of the QFT-Plus assay in 2018.

**11. Will the QFT In-Tube assay still be available in the U.S.?**

The QFT In-Tube assay will still be available, however, Qiagen plans to phase the assay out in June 2018. Reagents of the QFT In-Tube assay will be viable until June 2019, so laboratories may be using the QFT In-Tube assay until this time. The QFT In-Tube assay is no longer available in Europe.

**12. Where can I find more information on the QFT-Plus?**

For more information, see these links to the provider FAQ: [http://www.quantiferon.com/wp-content/uploads/2017/10/PROM-11186-001\\_1107785\\_BRO\\_QFT-Plus\\_GeneralSales\\_0717\\_US.pdf](http://www.quantiferon.com/wp-content/uploads/2017/10/PROM-11186-001_1107785_BRO_QFT-Plus_GeneralSales_0717_US.pdf)

Providers in LA County with questions about the QFT-Plus may also contact the LA County TB Control Program at 213-745-0800 and request medical consultation.

**References:**

1. QFT-Plus package insert: <http://www.quantiferon.com/wp-content/uploads/2017/10/QFT-Plus-ELISA-IFU-L1095849-R02.pdf>
2. QFT-Plus Provider FAQ: [http://www.quantiferon.com/wp-content/uploads/2017/10/PROM-11186-001\\_1107785\\_BRO\\_QFT-Plus\\_GeneralSales\\_0717\\_US.pdf](http://www.quantiferon.com/wp-content/uploads/2017/10/PROM-11186-001_1107785_BRO_QFT-Plus_GeneralSales_0717_US.pdf)
3. Telisinghe et al., “The sensitivity of the QuantiFERON-TB Gold Plus assay in Zambian adults with active tuberculosis”, IUATLD, 21(6), June 2017
4. Yi et al., “Evaluation of QuantiFERON-TB Gold Plus for Detection of Mycobacterium tuberculosis infection in Japan”, Scientific Reports, 6, 2016.