

## QuantiFERON® – reliable diagnostic information from the memory of our immune system

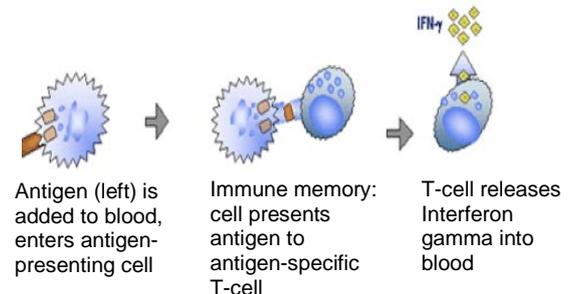


Among the technologies in QIAGEN’s portfolio that is transforming medicine is QuantiFERON – an innovative method for the detection of various pathogens including tuberculosis. QuantiFERON utilizes our body’s immune system to enable the detection of many diseases far earlier than possible with other methods, including DNA- and RNA-based molecular diagnostics. QuantiFERON is highly sensitive, allowing for the detection of

diseases in a latent or early stage, and has high specificity. In many cases, the technology can also be paired with nucleic acid-based tests.

Our pioneering QuantiFERON approach marshals the body’s own immune system to detect pathogens. The immune system comprises an army of cells that defend the body against invaders called antigens. It has specialized capabilities to recognize threats such as bacteria, viruses, cancer cells or toxins. Confronted by these “foreign” bodies, the immune system mobilizes and launches an attack. White blood cells and antibodies are designed to identify and destroy specific sites on antigens.

QuantiFERON tests take advantage of the immune system’s innate memory capacity. White blood cells called lymphocytes, more specifically T-cells, retain information about prior infections. When the same antigen is identified later, these antigen-specific T-cells release the signaling protein interferon-gamma (IFN- $\gamma$ ) to mobilize the body’s immune response. This level of induced interferon-gamma production can be measured.



A clinic using a QuantiFERON test begins by obtaining blood in QuantiFERON collection tubes specific to the targeted pathogen such as the *M. tuberculosis* bacteria. This blood is incubated in the collection tubes and, if the patient’s immune system has been exposed to the targeted pathogen, T-cells in the blood sample are re-stimulated and begin releasing interferon-gamma. The level of interferon-gamma is assessed in this way. QuantiFERON technology can identify the body’s immune response to pathogens and can be used as an aid\* to detect indirect infections that are present in such small amounts that they are not yet detectable with DNA- and RNA-based molecular diagnostics.

QIAGEN markets the QuantiFERON technology in several countries, including the United States and Europe, in various tests used for detection of tuberculosis infections and in transplantation medicine. International guidelines have expanded latent TB testing beyond developing countries and QIAGEN is working to ensure its continued global leadership with QuantiFERON.

## The modern standard for detection of tuberculosis infections

According to the World Health Organization (WHO), up to two billion people worldwide carry latent TB infection. If not treated, up to 10% of these individuals are at risk of developing the active form of the disease. Individuals with a weakened immune system are particularly at risk. Detection of latent TB is therefore an important component in the fight against the spread of this infectious disease, and the WHO's "Post-2015 Global Strategy" to fight the global TB threat incorporates latent TB screening of at-risk populations.

QIAGEN's QuantiFERON-TB Gold (QFT) is the modern standard for accuracy and ease of use in the indirect detection of TB infection. It is faster, and is more accurate than the tuberculin skin test (TST), a century-old technology for TB screening. Unlike the TST, the patient results can be obtained with a single office visit. Increasingly, the world's leading TB control programs are turning to QuantiFERON-TB Gold Plus to replace the skin test. The high clinical performance and the significantly simpler administration of QFT as a laboratory-based blood test, including integration with EMRs, combine to improve the cost-effectiveness of TB control programs and overall healthcare.

In 2015, QIAGEN launched QuantiFERON-TB Gold Plus (QFT-Plus), the fourth generation of the most accurate test to detect TB infections, in Europe and other markets. QFT-Plus provides for the first time a broader picture of the immune system's response to TB infections and is expected to set new standards for the management of this disease. The test incorporates CD8+ T cell response data to measure a broader range of immune response and has the potential to provide valuable new information to researchers, and comes with workflow improvements that allow even more efficient implementation, especially in large-scale TB screening programs.

In Spring of 2017, the company announced that new studies have shown the potential additional clinical value of QuantiFERON-TB® Gold Plus (QFT-Plus®). Both studies focus on the potential benefits of novel CD8+ T-cell stimulating antigens contained in QFT-Plus. A study at the Stanford University School of Medicine is the first publication describing the performance of QFT-Plus in healthcare workers, while a study at Japan's National Hospital Organization Hokkaido Medical Center provides the first evidence for QFT-Plus as a potential monitoring aid during treatment of active TB.

The QuantiFERON-TB tests are approved in many countries around the globe and recommended in several national and international guidelines. In mid-2017 the U.S. Food and Drug Administration approved QuantiFERON®-TB Gold Plus (QFT®-Plus), the company's fourth-generation Latent TB blood test. It combines breakthrough CD4/CD8 design for comprehensive immune response detection with the most flexible blood collection workflow. Some countries like South Korea are using QuantiFERON to control the disease in large groups in close quarters like their military. The technology is significantly more precise and easier to handle than the tuberculin skin test employed for latent TB detection over the past century. Consequently, the QuantiFERON-TB tests enjoy a growing popularity around the globe, leading the conversion of the global TB testing market from the TST.

[QuantiFERON-TB Access](#) (QFT® Access) is a proprietary new test designed to advance tuberculosis control in areas with limited infrastructure, including countries in Asia, Africa and Latin America. The World Health Organization (WHO) has classified 30 countries in these regions as high-burden, representing an estimated 85% of the global TB burden. QFT Access pairs highly sensitive digital detection with a complete workflow created to deliver cost-efficient results quickly

and with unmatched simplicity. It eliminates the need for an extensive laboratory infrastructure while providing best-in-class QuantiFERON technology. Clinical trials were conducted in 2019, and commercialization of QFT Access is expected to begin in 2020.

## Valuable molecular insights for better post-operative treatment of transplant patients

Worldwide, about 100,000 people annually receive a solid organ transplant. To reduce the risk of rejection, transplant patients receive a special immunosuppressive therapy following surgery. This treatment, however, increases their risk for potentially life-threatening infections, assigning a pivotal role to determining the right dosage of the immunosuppressive therapy.

QIAGEN's QuantiFERON technology addresses several challenges in the post-operative treatment of solid organ transplants:

- The QuantiFERON-CMV test helps healthcare professionals to determine the risk of potentially life-threatening infections with cytomegalovirus (CMV) by monitoring a patient's level of anti-CMV immunity. This test is CE-IVD marked.
- QuantiFERON Monitor is a novel test to assess an individual's cell-mediated immune response through dual innate and adaptive immune system stimulation following solid organ transplants. Currently, best practice in assessing immune reactivity is to monitor levels of those drugs. However, today there are no standard drug regimens applied to all patients and an estimated 40-70% of deaths following transplant surgery are attributable to issues with immunosuppression or immunosuppressants. QuantiFERON Monitor thus addresses an urgent medical need and provides healthcare professionals important information on the strength of the immune system in the immunosuppressed solid organ transplant patients. This test is CE-IVD marked.

*\*QuantiFERON®-TB Gold (QFT®) is an in vitro diagnostic test intended as an aid for the indirect detection of Mycobacterium tuberculosis infection and is for use in conjunction with risk assessment, radiography, and other medical and diagnostic evaluations. QFT results alone cannot distinguish active TB disease from latent infection.*