



Update on Xpert MTB/RIF

FIND is pleased to announce that, since its endorsement by WHO in December 2010, the Xpert MTB/RIF test co-developed with Cepheid has attracted great attention from disease-endemic countries, health-care professionals, media, civil society and donors. In the first month since the endorsement, 77 countries have made enquiries about orders of the test, with many countries having received at least one delivery already.

While we are excited about this growing interest, FIND remains committed to working with WHO to address any challenges that arise during this post-endorsement phase. A few questions have been brought to our attention, and I thought I would provide some clarifications to all our partners on the following topics:

Temperature

The recommended storage temperature for the Xpert MTB/RIF cartridges is currently 2-28°C. The maximum recommended ambient operating temperature of the GeneXpert system is currently 30°C, based on extensive validation studies. Demonstration studies conducted by FIND in higher temperature settings over the past 18 months did not show any decrease in performance or quality.

To protect the integrity of the GeneXpert thermal cycling capability and ensure robust assay performance the system automatically monitors the internal temperature of the instrument. If the internal temperature of any idle module in the GeneXpert system exceeds the recommended operating temperature by 5-10°C (due to elevated ambient temperature), the module becomes temporarily unavailable for use. If the internal temperature of a module exceeds the recommended operating temperature by 5-10°C during a test, an error message is automatically produced and the test in process is reported as ERROR. Once the internal temperature drops back to the recommended ambient temperature conditions, the system function returns to normal.

The only instrument failure recorded in the demonstration studies was unrelated to temperature.

We recognize that many disease endemic settings may have higher ambient temperatures. We are therefore actively working with Cepheid to investigate the possibility of extending the recommended operating conditions for the GeneXpert system and the storage conditions for Xpert MTB/RIF cartridges. Furthermore, it is important to note that testing kits and reagents currently in wide-spread use for other disease programmes at similar levels of the health system (e.g. for HIV viral load and CD4+ tests) usually have similar or lower temperature storage requirements.

FIND and WHO's Global Laboratory Initiative are establishing a programme for post-marketing surveillance of any Xpert MTB/RIF adverse events, results of root cause analyses and corrective action. WHO will share this information on its website to ensure that partners have access to this critical data in a transparent and timely manner.

Electricity

The GeneXpert system requires a relatively stable, clean, uninterrupted electric supply when it is in use. It is recommended to connect the system to a 400VA UPS device which delivers conditioned power, with the ability to support interruptions of up to 15 minutes.

Test accuracy

Evaluation and demonstration studies conducted in nine countries by FIND and partners have shown that the sensitivity of Xpert MTB/RIF was equivalent to solid culture¹. The overall sensitivity of a single, direct Xpert MTB/RIF was 90%, compared to 89% for a single LJ solid culture [when compared to a reference of two solid and two liquid cultures per patient]. The sensitivity among smear-negative patients was 70-80% with a specificity of 99%. Rifampicin resistance was detected with 95% sensitivity and 98% specificity using a single test.

Price

For almost 150 low-income and disease endemic countries, the ex works price per cartridge is currently \$16.86, with a FIND negotiated agreement to reduce this price as global volumes increase. The GeneXpert GXIV-4 configuration (which can take up to 4 cartridges at a time) is priced at \$17,000-\$17,500 (ex works). This price was negotiated by FIND and represents a significant reduction when compared to the manufacturer's list prices in Europe and the USA.

The prices of these machines and reagents have sometimes been compared to the average \$1-2 per single smear microscopy slide. It is acknowledged that the price of an Xpert MTB/RIF test is significantly higher than a single microscopy test; however, it should be kept in mind that Xpert MTB/RIF has much higher accuracy than microscopy and also detects rifampicin resistance. A cost comparison with conventional culture and drug susceptibility testing shows that the unit cost of performing the Xpert MTB/RIF test is in the same range. A cost-effectiveness study by the Amsterdam Institute of Global Health and Development in The Netherlands shows that Xpert MTB/RIF is likely to be a cost-effective investment for TB programmes.

Further costing models developed by WHO's Stop TB Department show that the global costs of rolling out Xpert MTB/RIF by 2015 could represent between 1% of global TB control costs (if it is used as an MDR-TB screening tool) and 13% (if it replaces smear microscopy).

Xpert MTB/RIF prices are also comparable, and sometimes significantly lower, than the prices of tests such as HIV viral load or CD4+ that have been successfully rolled out around the world, and are routinely performed at a similar level of the health system.

¹ Boehme C, Nabeta P, Hillemann D *et al*, Rapid Molecular Detection of Tuberculosis and Rifampicin Resistance, *New England Journal of Medicine*, 2010; 363:1005-1015.