



THE VISION.... “A Better Way to fight TB”

Global headlines around the world have praised the potential impact of Cepheid’s GeneXpert® and Xpert® MTB/RIF test in the fight against TB. *“It’s completely changing the way people think about how to diagnose TB.”*

Since the endorsement by the World Health Organization in December 2010, global interest in deploying this powerful new technology in the fight against TB continues to grow at a rapid rate.

A question that commonly arises is concern about pricing and affordability in the High Burden Developing Countries (HBDC).

In the interest of transparency, Cepheid has prepared the following background summary to help interested parties at all levels (Ministries of Health & Donor Organizations) understand the facts on the following topics:

- How was the GeneXpert and Xpert MTB/RIF test developed?
- What was the source and extent of external funding for development of the Xpert MTB/RIF test?
- What was Cepheid’s contribution to the foundational technology that enabled the Xpert MTB/RIF test?
- How is the price determined for the GeneXpert System and Xpert MTB/RIF test sold to the HBDC Market?
- What are the most important factors influencing the price of the GeneXpert and Xpert MTB/RIF test going forward?

Key Milestones in the Evolution of the Xpert MTB/RIF test:

□ **May 22, 2006** Cepheid and Foundation for Innovative New Diagnostics (FIND) entered into a Cooperative Research and Development Agreement (Cepheid-FIND 2006 Agreement) to develop a simple, rapid diagnostic test to be run on the GeneXpert

System that could detect Mycobacterium tuberculosis and associated rifampin resistance from human sputum samples.

FIND selected Cepheid for this collaboration after conducting extensive due diligence across the molecular diagnostic industry. FIND recognized the potential value the GeneXpert platform could bring to the diagnosis of MTB and rifampin resistance in the HBDC Market even though the system was not fully developed at that point in time

Since its inception, Cepheid's objective has been to develop the unique technology of the GeneXpert System as "A Better Way" for healthcare institutions worldwide to realize the benefits of molecular diagnostics. This benefit has definitively been realized in its application to TB within the HBDC Market.

- **April 2009** – Xpert MTB/RIF test released under European CE-IVD marking;
- **May 2009** – FIND Demonstration studies underway;
- **September 2010** – New England Journal of Medicine publishes validation data; an Expert Group issues strong recommendation to WHO based on scientific evidence; WHO's Strategic and Technical Advisory Group (STAG) for TB further reviews evidence and makes policy recommendations;
- **November 2010** – WHO global consultation develops roadmap for implementation of the Xpert MTB/RIF;
- **December 2010** – WHO endorses Xpert MTB/RIF;
- **March 2011** – WHO Publication of Rapid Implementation of the Xpert MTB/RIF diagnostic test: Technical and operational 'How-to' Practical considerations, providing guidance on diagnostic algorithms, site selection, and operational considerations

The Collaborative Development:

The development of the Xpert MTB/RIF test truly represents what can be accomplished in a successful "Academic-Public-Private Partnership".

Participants in this Partnership included:

- Cepheid
- Foundation for Innovative New Diagnostics (FIND)
- University of Medicine and Dentistry of New Jersey (UMDNJ)

- National Institute of Allergy and Infectious Diseases (NIAID)

Funding for this project was supplemented by FIND and the NIAID. These private and public funds were leveraged across the significant R&D investment made by Cepheid in the foundational technology embodied in the GeneXpert and the Xpert Cartridges. It is important to point out that the current embodiment of the GeneXpert System and the Xpert test cartridge design did not exist at the time of the TB project initiation in 2006. As such, the project was dependent on Cepheid incrementally investing and successfully developing these key aspects of the overall system above and beyond the portions of the project contributed by the partners.

Foundational Technology Funding:

Cepheid has invested over **\$300Mil USD** to date in the development of the foundational technology that enabled the creation of the GeneXpert platform and Xpert MTB/RIF test, including but not limited to:

- The Cepheid patented GeneXpert Platform to run the test (Scalable from the single module GX1 to the GX2, GX4, GX16, Infinity 48 and Infinity 80).
- The Cepheid patented Xpert Cartridge Technology that radically simplifies sample preparation, amplification and detection.
- The Cepheid Proprietary Chemistry and Manufacturing Processes (Probes, Primers, Fluors, Quenchers, Binding Chemistry, etc).
- The Automated Xpert Cartridge Manufacturing Lines and the unique ability to package liquid and dry reagents within the same container while maintaining reagent stabilities of twelve months and longer.
- In-licensed technology required for Freedom of Operation under third party patent rights.
- Global Regulatory Submissions:

Xpert MTB/RIF Development Funding:

To date, approximately **\$37Mil USD** has been invested in the development of the Xpert MTB/RIF test by Cepheid, FIND and NIAID.

Of these investments:

- Non-Cepheid contributions for the development of the Xpert MTB/RIF were approximately **\$12Mil USD** originating from the following:
 - Cepheid-FIND 2006 Agreement
 - NIAID Grants
- Cepheid's contribution for the Xpert MTB/RIF test development was in excess of **\$25Mil USD** for the separate activities summarized below:
 - The 6 Color Project
 - Liquid Reagents On-Board
 - Development of the Reagents on Board Assembly Line
 - Continuous Product Improvement of the Xpert MTB/RIF test
 - Global Regulatory Submissions

Pricing to the FIND Target Market of 145 Countries :

In exchange for FIND's funding in this collaboration, Cepheid agreed to provide Special Pricing for all 145 FIND Target Market Countries in the HBDC Market as defined under the Cepheid-FIND 2006 Agreement and published on the FIND website:

- The Cepheid-FIND 2006 Agreement provides pre-negotiated, preferential pricing uniformly across ALL 145 Countries in the HBDC Market. This pricing resulted in significantly discounted access to the GeneXpert GXIV-4 and the Xpert MTB/RIF tests when compared to Cepheid's commercial pricing.
- As a point of reference:
 - The Commercial Price of the Xpert MTB/RIF test is 50 Euros (\$71.63 USD) while the product is currently available to the HBDC Market at the ExWorks price of \$16.86 USD (a 76% discount off of the Commercial Price).
 - The Commercial Price of the GeneXpert GX4-4 is \$78,200 USD while the system is currently available to the HBDC market at the Ex-Works price of \$17,000 USD (a 78% discount off of the Commercial Price).

To give some context to the financial impact of this preferential pricing, Cepheid has granted a discount of over **\$18Mil USD** under the Cepheid/FIND Agreement on sales of GeneXperts and Xpert MTB/RIF tests in the FIND Target Market from 2010 through Q2 2011.

This initial savings of **\$18Mil USD** represents a significant return on the combined external investment by FIND and NIAID of **\$12Mil USD**. This investment will continue to pay dividends not only in the dollars saved (through preferential pricing) but much more importantly in the thousands of lives saved. Cepheid does not wish to diminish the importance of this initial funding for without it this project would never have gotten off the ground. However, this external funding is only a small part of the overall investment required to bring the Xpert MTB/RIF test to market. Cepheid continues to invest in the on-going improvement of the Xpert MTB/RIF test as well the foundational technology to the benefit of all who are in the process of adopting the test today.

How is the Price of the Xpert MTB/RIF test determined?

The ExWorks price of the Xpert MTB/RIF test to the 145 Countries in the HBDC Market is determined under the Cepheid-FIND 2006 Agreement by the following formula:

ExWorks Price to the Find Target Market = (Cepheid's Manufacturing Cost) + (20% mark-up) + (royalties if applicable) + (distributor mark-up if applicable¹)

- Cepheid's Manufacturing Cost is defined as the fully-burdened manufacturing cost of a product and is calculated in accordance with U.S. Generally Accepted Accounting Principles (GAAP) and includes direct materials, direct labor, and fixed and variable manufacturing overhead, cost of quality control, product testing, manufacturing variances and other cost that may be properly attributed to inventory as manufacturing costs pursuant to GAAP (but not including royalties, fees or similar considerations paid to Third Parties for rights to Intellectual Property, including up-front payments for such rights).
- Cepheid updates the Manufacturing Cost and the resulting ExWorks price annually at the beginning of the calendar year. The resultant updated cost is primarily driven by the total volume of tests to be produced during the

¹ Distributor mark-up is typically 5% for the Xpert MTB/Rif test and 10% for the GeneXpert instrument.

subsequent year. This process is subject to external audit in accordance with the Cepheid-FIND 2006 Agreement.

What are the most important factors influencing the price of the test going forward?

The single most influential factor impacting the price of the test going forward is test volume. Higher annual test volume will directly translate into lower overall production costs and result in a lower ExWorks price to the HBDC Market.

Another important factor is the royalty burden. From the beginning, Cepheid has worked with partners from whom Cepheid licenses intellectual property to minimize or in some cases eliminate many of the royalties that impact both the Xpert MTB/RIF test and GeneXpert platform for the HBDC Market. As some of the licensed patents expire the royalty burden will be further eased and this benefit will be passed through in the form of lower pricing.

Would regional manufacturing have any impact on the price of the test?

Cepheid has invested significant resources to expand our US manufacturing facility in California with a mirror facility located in Stockholm, Sweden to meet the increased global demand for Xpert test production. Cepheid's production methods are totally unique and highly automated. As such, the direct labor component of the Cepheid process represents a very small percentage of the total cost of the product. The overwhelming majority of product cost resides in material and overhead which is only impacted by total test volume demand. Regional manufacturing beyond that already established by Cepheid would have little to no impact on the price of the test and would more likely result in an increase in test cost due to increased overhead spending and lower absorption of the cost of manufacturing facilities.

Would Cepheid consider licensing the Xpert technology for generic test production?

As previously noted, Cepheid has expended well in excess of **\$300Mil USD** in the foundational technology that makes the GeneXpert and Xpert cartridge a reality. This technology is embodied in a family of patents, trade secrets and proprietary

manufacturing processes developed and held exclusively by Cepheid. Licensing is thus not an avenue that would be viable for the Cepheid Xpert MTB/RIF test.

Cepheid's clinical products are delivered globally with the highest degree of quality and consistency as required under CE-IVD and FDA. Our customers can be confident that the same test ordered anywhere in the world will produce identical results. Cepheid will not compromise on quality or performance nor will we produce an inferior product to serve the HBDC market.

It should also be recognized that the GeneXpert System is virtually capable of testing for any type of infectious disease and other genetic based diseases. As such, High Burden Developing Countries deploying the GeneXpert System for TB today may also be able to obtain substantial incremental benefit tomorrow through use of the installed base of systems for other tests of specific interest such as HIV viral load (an active Cepheid/FIND Collaboration).

Cepheid Cares:

For other updates on Cepheid's GeneXpert and the Xpert MTB/RIF test please refer to the Cepheid Cares website: <http://www.cephidcares.com/tb/index.html>