A new resource for TB diagnostics developers

"Considerable efforts are being made to understand and document frequently asked questions of greatest importance to TB diagnostics developers, and efforts are being made to address them using the website resource created."

Zhi Zhen Qin[1] & Madhukar Pai*[1]

[1]McGill University, Department of Epidemiology & Biostatistics, 1020 Pine Avenue West, Montreal, QC, H3A 1A2, Canada

*Author for correspondence: Tel.: +1 514 398 5422 ■ Fax: +1 514 398 4503 ■ madhukar.pai@mcgill.ca

Editorial

Future Microbiology

In 2013, TB remains a major public health concern, with over 8 million new cases occurring annually [1]. Although many countries have met the Stop TB targets of 70% case detection and 85% cure, the incidence of TB is declining very slowly. It is clear that unless TB is detected early and treated promptly, it will be difficult to interrupt transmission and reduce incidence [2]. This will require more accurate diagnostics than what we have today, as well as approaches to engage first-contact providers to reduce diagnostic delays and detect TB early.

Fortunately, the past few years have been a boom period for TB diagnostics development, with several new and improved technologies now available on the market [101] and endorsed by WHO [3]. One of them, the Xpert® MTB/RIF test (Cepheid Inc., CA, USA), was endorsed by WHO in 2010 [3] and has high accuracy [4]. It is being actively rolled out in many countries, with over 3 million tests used in over 80 countries [102]. Inspired by the success of this molecular test, there is considerable industry interest in TB product development – there are more than 50 diagnostic companies operating in this space [5,6].

The TB community now needs to keep the momentum going and continue to promote innovation in product development so that more accurate and affordable diagnostics can be developed and scaled-up. Often the greatest challenge for assay developers and manufacturers is not science or engineering, but knowing what products are really needed in the market and would be economically viable, knowing how to position their product in the market, and understanding the regulatory and policy complexities.

To address the information gaps among product developers, we recently conducted an informal survey of more than 25 test developers and manufacturers to identify the questions that they deemed the most relevant to TB product development and commercialization [5,6]. We organized the questions we identified according to the stages of development and categorized them into ten frequently asked questions (FAQs):

- TB burden and treatment landscape: what is the global burden of TB (including latent TB, TB and HIV coinfection, and drug-resistant TB) and what is the current and future TB treatment landscape?
- Current diagnostics landscape and pipeline: what is the current testing landscape for TB (including latent TB and drug-resistant TB) and what diagnostics are in the pipeline? What is the level of access to current TB diagnostics and what are the gaps?
- Market size, potential and dynamics: what is the market size and potential for new TB diagnostics, and what are the market dynamics around TB diagnostics?
- Target product profiles (TPPs): what are the unmet diagnostic needs and TPPs of greatest relevance or priority?
- Product development support: where and how can test developers and companies find funding and technical assistance, and secure necessary specimens/strains for test development and quality control?
- Product validation support: what kind of validation is required for a new TB diagnostic to enter the market and where can companies obtain support for such validation?
- Regulation: what are the regulatory requirements for TB diagnostics, both in-country and globally?
- Policy: are global policy endorsements required? If so, what kind of evidence is

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necessary for global policy endorsements and scale-up?

- Procurement and market access: how do countries procure TB diagnostics? How much is procurement influenced/guided by WHO and/or donors?
- Scale-up: once a product has been validated, registered and put on the market, and once policy endorsements have been obtained, what are the challenges for uptake and scale-up?

To answer these FAQs and share relevant documents, we then created an open-access website resource [103]. This website describes the ten FAQs, along with more nuanced questions raised by product developers, and provides some answers and useful documents for each of the ten FAQs. To ensure that our responses to the FAQs met the needs of product developers, we consulted various stakeholders and asked them to comment on the website and provide input. Their opinions and feedback were addressed in subsequent versions of the site.

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Some of the FAQs could be answered easily. For example, global TB reports from WHO provide good data on the TB epidemic and burden, and likely trajectories of the global epidemic [1]. A series of technology and market landscape reports by UNITAID [104] provide the most up-to-date information on the current TB diagnostic landscape and pipeline [7,8]. As newer nucleic acid amplification tests have emerged to fill the need for a more decentralized setting [9] as compared with Xpert MTB/RIF, surveys have been conducted to describe the status of peripheral microscopy centers in 22 high-TB-burdened countries [10]. The current WHO policy process for TB diagnostics and regulatory requirements of diagnostics in many countries are also described on the website, which also provides information on where product developers can access TB specimens [103].

However, answers to the other FAQs require research that is either ongoing or will need to be conducted. The previous global TB market analysis [11] conducted by the Foundation for Innovative New Diagnostics [105] and WHO almost 10 years ago needs to be updated, as several new technologies have emerged since it was published. Indeed, assay developers are keen to learn the market potential for new products, after accounting for the roll-out of Xpert MTB/RIF. In other words, how much of the market is addressed by Xpert MTB/RIF and how much remains? In addition, efforts are needed to capture the current market segmentation, such as the public versus private split, the market size for drug-susceptibility testing, treatment monitoring and latent TB infection (for preventive therapy), and other niche markets for pediatric TB, individuals living with HIV, among others.

Emerging economies are now the focus of attention, especially China, India, Brazil and South Africa. These four countries alone account for more than half of the global TB burden. In addition, these nations are also heavily investing in TB control and are becoming early adopters of new tools. For example, South Africa has scaled-up the Xpert MTB/RIF technology across the entire country and over 1.5 million tests have been used since the roll-out began in 2011 [102]. However, the value chain for policy and uptake of new technologies within these countries is not transparent, and this can be a roadblock for scale-up [12].

To account for all the new developments and shifts in the diagnostic landscape, efforts are now underway to assess the served available market for TB diagnostics in India, China, Brazil and South Africa, addressing their specific market potential and challenges. This work, supported by the Bill and Melinda Gates Foundation, UNITAID, FIND and other in-country partners, is expected to be completed by early 2014 [8].

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Another important information gap to be addressed is the development of TPPs for new TB tests, especially those intended for point-of-care testing programs, where the goal is to ensure rapid completion of the test and treat cycle in the same clinical encounter [13]. Again, efforts are underway to identify, prioritize and develop detailed TPPs that are most critical for TB control and will have a good market potential. Currently available TPPs have been compiled [103].

In summary, considerable efforts are being made to understand and document FAQs of greatest importance to TB diagnostics developers, and efforts are being made to address them using the website resource created [103]. By organizing the information and compiling it on one website, we hope to address critical information gaps in the field and inspire more vigorous product development efforts. By making information more accessible and searchable, we hope academics as well as smaller companies and startups will be encouraged to enter this field and make a positive contribution to TB control.

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