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EDITORIAL

Tuberculosis diagnostics: test developers' FAQs

WITH THE RAPID EXPANSION of the tuberculosis (TB) diagnostics pipeline, the reduction in the price and roll-out of Xpert® MTB/RIF technology (Cepheid Inc, Sunnyvale, CA, USA), and increases in donor investments (especially in biomarker discovery), there is for the first time considerable industry interest in TB diagnostics.[1] Four new 'fast-follower' molecular tests are now on the market, and more than 50 diagnostic companies and test developers are actively engaged in TB technologies. With the recent US Food and Drug Administration approval of Bedaquiline, there is renewed interest in developing drug susceptibility testing (DST) methods for new TB drugs. These trends are quite remarkable given the historical lack of industry investments in TB.

A key issue for the wider TB community is this: now that industry interest in TB is at an all-time high, how do we sustain the momentum, and support these test developers in developing more tools for TB? The answer is by identifying their greatest needs and questions, and by answering them in a clear, credible, transparent manner.

An informal survey of over 25 test developers revealed several critical questions:[2]

1 What is the global burden of TB (including latent TB, TB and human immunodeficiency virus [HIV] co-infection and multi- and extensively multidrug-resistant TB), and what is the current and future TB treatment landscape?
2 What is the current testing landscape for TB (including latent TB and DST), and what diagnostics are in the pipeline? What is the level of access to current TB diagnostics?
3 What is the market size and potential for new TB diagnostics, and what are the market dynamics around TB diagnostics?
4 What are the unmet diagnostic needs and target product profiles (TPPs) of greatest relevance?
5 Where and how can test developers and companies find funding and technical assistance and secure necessary specimens/strains for test development and quality control?
6 What kind of validation is required for a new TB diagnostic to enter the market, and where can companies obtain support for such validation?
7 What are the regulatory requirements for TB diagnostics, both in-country and globally?
8 Are global policy endorsements required? If so, what kind of evidence is necessary for global policy endorsements and scale-up?
9 How do countries procure TB diagnostics? How autonomous is their decision making? How much is it influenced/guided by the World Health Organization and/or donors?
10 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?

Beyond these high-level questions, test developers have nuanced questions. For example, what is the likely trajectory of the TB epidemic and future patient demographics over the next 5–10 years? What is the treatment landscape likely to be in the next 5–10 years? What are the market potential and barriers for new tests, after accounting for the roll-out of Xpert MTB/RIF? What needs do technologies such as Xpert MTB/RIF meet? How much of the market will they address? What problems remain? And how much are purchasers willing to pay for new TB tests?

While some of these questions have been addressed in previous market analyses and needs assessments,[1,3–5] updated analyses are necessary to support product development in today's rapidly evolving landscape. They can convince industries and investors about the need and market for new TB tools, help develop TPPs that can guide product development and scale-up, and guide donor/funder decisions.

Test developers are particularly keen to learn about the most important TPPs, and which TPP attributes really matter. What four to five features are most needed in a TB diagnostic test for developing countries? Attributes include target cost (what are countries or purchasers willing to pay?), sensitivity/specificity, infrastructure requirements, time to result, throughput, sputum vs. other samples, manual vs. automated, requirements for reporting of test results, point-of-care vs. centralized laboratory testing, integrated or reflex DST, which drugs to include in DST, TB-only test vs. multiplexed platform, instrument/test connectivity requirements, and importance of subgroups such as HIV-infected patients and children.

Although there is widespread agreement that a simple point-of-care test is urgently needed,[4] there is no consensus on which TPP attributes will have the greatest impact on reducing the incidence of TB in disease-endemic countries. There is also awareness that point-of-care testing is a spectrum—a single TPP may not be able to fulfill the needs of patients, providers and laboratory workers across a multitude of settings and uses (triage, diagnosis, monitoring and DST).[6]

To help advance the field, a new website resource has been created to identify and answer major frequently asked questions (www.tbfaqs.org). It is now important that we answer these questions, make them

available in one place, and create an active community of users who can share insights and answers. While some questions can be answered easily (e.g., current TB burden), others require work (e.g., current market size and TPPs of greatest relevance). For some questions, test developers will need to do their own research and build an investment case.

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