TB diagnostics: top 10 FAQs by test developers

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The TB dx landscape in 2012 is quite remarkable

- Tuberculin
- Conventional microscopy
- Solid cultures
- Conventional, phenotypic DST
- Conventional PCR
- IGRAs
- LED/FM microscopy
- Liquid cultures
- Molecular DST (LPA)
- Cartridge-based NAATs
But

- We still have big unmet diagnostic needs
- We need better and more affordable tools
- We need competition to increase affordability and diversity of options
Thankfully

- Fast-follower NAATs are rapidly emerging
- Big investments made in biomarkers for POC solutions
- Unprecedented industry interest
  - Revival of interest among established players
  - New players, including those from emerging economies
- We must encourage and support these product developers
Engaging industries and donors in emerging economies

TB diagnostics in India
From importation and imitation to innovation

August 25 – 26, 2011
Bangalore, India

Host: St. John’s Research Institute, Bangalore, India
Sponsors: McGill University & Global Health Strategies
Technical partners: Bill & Melinda Gates Foundation, Foundation for Innovative New Diagnostics, International Centre for Genetic Engineering and Biotechnology (IGEB), India & Stop TB Partnership
Industry partners: Association of Biotechnology Led Enterprises (ABLE) & Confederation of Indian Industry (CII)
Media partners: BioSpectrum Asia, Express Pharma & Express Healthcare

Context and rationale
The scale-up of DOTS in India is a great public health accomplishment, and yet undiagnosed and poorly managed TB continues to fuel the epidemic. Recognizing these challenges, the Government of India has set an ambitious goal of providing universal access to quality diagnosis and treatment for all TB patients. Innovative tools and delivery systems in both the public and private sectors are critical for reaching this goal. The current in-vitro diagnostics market in India is dominated by imported and generic products, with virtually no innovations. But India has the potential to solve its TB problem with "home-grown" solutions, just as Indian pharma and biotech companies revolutionized access to high-quality, affordable AIDS drugs and hepatitis vaccines through generic production. Indian diagnostic companies could also become the world’s hub for high-quality generic diagnostics. India also has the potential to lead the world in developing innovative TB diagnostics. For this to happen, Indian industry must move from the import and imitation approach to genuine innovation in both product development as well as delivery. This will require supportive policies, enhanced funding, and collaboration between government, donors, researchers and the private industry. The goal of this conference is to engage these stakeholders to stimulate interest and investments in TB innovations.

Bangalore 2011
http://gongyi.qq.com/zt2012/Diagnostics/

Shanghai 2012
Test developers are asking important questions

• Based on input from over 25 companies and test developers (including academics), here are the top 10 FAQs
  • Follows a natural order: Current landscape, market, unmet needs, TPPs, product development, evaluation, regulation, policy and scale-up

I am very grateful to these individuals and companies for their candid and detailed responses!
#1. TB BURDEN AND Rx LANDSCAPE

What is the global burden of TB (including latent TB, TB/HIV and MDR/XDR-TB) and what is the current and future TB treatment landscape?

- What is the current burden and predictions for future, disease distribution (highest burden countries), current and future patient demographics, and trends over the next 5-10 years?
- What is the treatment landscape today and in 5-10 years? What is the level of access to current TB treatment?
- What TB drugs are currently important for drug susceptibility testing (DST), and which drugs will need to be considered for DST in the near future?
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?

- What TB diagnostic tests are currently on the market, and what products are likely to enter the market in the near future?
- Which tests are currently included in policy recommendations and widely used? What are the currently used diagnostic algorithms? Who develops them and what is the process for changing the algorithm?
- What is the current level of access to available TB diagnostics in high burden countries?
What is the market size and potential for new TB diagnostics, and what are the market dynamics around TB diagnostics?

- What is the current market size for TB diagnostics? What is the market potential for new tests? What is the expected market growth rate?
- How is the market segmented by low, middle vs. high income countries? By where the test might be utilized (i.e. reference lab, microscopy center, etc.)?
- How is the market served currently? What are the key market barriers for uptake? What will drive uptake?
- Will most high burden countries scale-up Xpert MTB/RIF? What needs does it meet? How much of the market will it address? What problems remain?
- Are market access barriers lower for 2nd or 3rd, rather than the 1st product in its class?
- What is the risk for new products that have to compete against entrenched competitors?
#4. TARGET PRODUCT PROFILES

What are the unmet diagnostic needs and target product profiles (TPPs) of greatest relevance?

• Which attributes within the TPP are the most important to focus on? What are the top 4-5 features that are needed in a TB diagnostic test for developing countries?
  
  • At what price/cost can a new TB diagnostics be sold? What is the current and projected pricing environment over the next 5-10 years? Is the $9.98 price the new benchmark?
  • What are the differences in the market opportunities for a screening test and separately for a DST? How is the price/cost affected if the new test is a screening (broadly used) test versus an “add-on” or reflex test?
  • How critical is it to include DST in the test? Which drugs are critical for DST now, and in the future? Is it advantageous to have a platform that can detect a large number of mutations? What is the cost-benefit ratio of having these additional elements in the test?
#4. TPP attributes

- Target cost
- Sensitivity/specificity (which is more important and minimum acceptable levels)
- Point-of-care versus centralized lab testing
- Manual versus automated
- TB only test versus multiplexed platform (e.g. + HIV, CT/NG)
- Integrated or reflex DST
- Rule-in or rule-out test?
- Infrastructure requirements (e.g. power, temperature control)
- Time to result (how important is same-day results?)
- Throughput
- Sputum versus other samples
- Requirements for reporting and connectivity
- Drugs to include in DST
- Importance of subgroups such as HIV-infected and children
- Shelf-life requirements, etc.
#5. PRODUCT DEVELOPMENT SUPPORT

Where and how can test developers get funding, technical assistance and secure necessary specimens/strains for test development?

- How do companies get funding for TB dx development?
- Which are the key funding/donor agencies (e.g. NIH, BMGF, USAID, DFID, Wellcome) and what are their funding priorities in product development?
- If donors support product development, what are their expectations in terms of pricing, global access, IP, etc.?
- Which are the PDPs (e.g. FIND, PATH, IDRI) that can provide support with TB dx development and what are their criteria/conditions for providing support?
- Where can test developers get well-characterized specimens (including non-infectious artificial sputum), strains, sequences for DR mutations and BSL3 facilities?
#6. PRODUCT VALIDATION SUPPORT

What kind of validation is required for a new TB diagnostic in order to enter the market and where can companies get support for such validation?

- How many validation studies will be required? Are test accuracy studies adequate, or clinical impact studies required? How much geographical diversity is needed for the clinical trials?
- What validation studies were required for, and conducted by Cepheid to bring their TB test to market? How much did it cost and who paid for it?
- Who can provide clinical trials and validation support to companies?
- What will it cost to conduct clinical validation studies? Will donors pay for product validation?
- Which academic institutions are capable of test validation and field trials?
- Which are the PDPs (e.g. FIND, PATH, IDRI) or agencies (e.g. CDRC, CHAI) that can provide support with validation and what are their criteria/conditions for providing support?
#7. REGULATION

What are the regulatory requirements for TB diagnostics, both in-country and globally?

- What is required for the registration of new diagnostics in the major, high TB burden countries?
- Will multiple regulatory approvals be necessary? What will it cost? Is there a pathway to get simultaneous approvals?
- How critical is FDA approval for global markets and what will it take to get FDA approval?
- What are the advantages and disadvantages of getting CE mark versus WHO PQ versus FDA approval and which of these is needed for major markets?
- How strong is the IP in the TB diagnostics area?
#8. POLICY

Are global policy endorsements required? If so, what kind of evidence is necessary for global policy endorsements and scale-up?

- What global policy endorsements or approvals are critical for success (e.g. WHO, CDC, FDA, others)?
- Is WHO endorsement/policy the most important factor for accessing global markets? What is the timeline and cost for WHO process? How does WHO decide on which technologies to consider for policy review?
- Is there a WHO PQ process for TB diagnostics, and if so, how long will it take? What is the difference between WHO policy and WHO PQ for TB?
- What kind of evidence is required at the country level to get policy endorsements and registration? Is WHO endorsement or prequalification alone sufficient? Are country evaluations still required?
How do countries procure TB diagnostics? How autonomous is their decision making? How much is it influenced/guided by WHO and/or donors?

- Who are the major buyers in developing countries (e.g. Ministries of Health (MoH), National TB Programs (NTPs), international donors)?
- What are the most important MOH concerns, and how does the MOH procure, direct procurement, and make decisions on vendors?
- What are the market access challenges and options for addressing them? Is procurement linked to regulatory approval? Will each country require an independent study of a TB diagnostic?
- What are the logistics and distribution challenges? Different for public vs. private sector, or is there a single centralized process in countries?
- What will be required by developers/suppliers to provide sales and after-sales support, as well as service and maintenance?
Once a product has been validated, registered and put on the market, and once policy endorsements are obtained, what are the challenges for uptake and scale-up in high burden countries?

- Which validated tests have been successfully scaled-up, what were reasons for the success, and how long did it take to reach scale?
- How do country level policy makers make decisions on tests to scale-up?
- If some tests have not been scaled-up even after policy endorsements, why? What are the biggest barriers and how can they be overcome?
- When and how do donors fund/subsidize and support roll-out of TB diagnostics?
  - Who are the major players in funding scale-up (e.g. UNITAID/ GFATM/BMGF/PEPFAR/USAID), and their historical role and funding mandate/priorities?
  - Since donors are already supporting the roll-out of GeneXpert, will they consider other technologies for buy-down and/or scale-up?
  - Is WHO endorsement mandatory for donor support for scale-up?
  - What are the long-term prospects after donor funding ends?
  - Are there markets that are not dependent on donor funding?
Answering these FAQs will make a big difference to test developers

• “If we can help get this info out, more people will consider developing TB products…”

• “these questions are very good and we have had to learn the answers the hard way!”

• “great idea to put them together… when we first started with TB, we had no idea about any of this. I think it will be a tremendous help especially for the smaller companies out there who are perhaps new to the entire diagnostics…”

• “top ten FAQ is a fantastic idea! we spent much of our time trying to understand these particularly nuanced areas in shaping our business case.”

• “If we had the answers to those questions, it would have saved us lots of time…”

• “having had access to such information would have had a very positive impact on our development and it would have helped us to correctly set our internal expectations.”
Why haven’t we addressed these FAQs already??

- Well, we have answered them, in bits and pieces

  - May not be perfect or nuanced
  - May not answer all questions
  - May need to be updated/revised in light of rapidly changing landscape

- For some questions, I am not sure we know the answers!
Global TB burden and Dx landscape


http://www.pipelinerreport.org/toc/tb-diagnostics
Market size, potential and dynamics

FIND/TDR 2006

TPPs – some exist, but which will be most impactful?

POC test (MSF/TAG/STP)*

POC triage test

Simple and affordable molecular dx

High throughput molecular dx for centralized labs

Unmet needs and research priorities


http://www.stoptb.org/global/research/
Value chain and evidence required

NDWG 2010

http://www.stoptb.org/wg/new_diagnostics/
IVD regulation and harmonization


Post-policy scale-up challenges

Making innovations accessible to the poor through implementation research


New tuberculosis technologies: challenges for retooling and scale-up

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Policy Forum

Point-of-Care Testing for Infectious Diseases: Diversity, Complexity, and Barriers in Low- And Middle-Income Countries

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StopTB Partnership

INTRODUCING NEW APPROACHES AND TOOLS FOR ENHANCED TB CONTROL (INAT) SUBGROUP

http://www.stoptb.org/wg/dots_expansion/inat.asp
What we need

• More cohesive, credible, up-to-date answers to these FAQs, in the post-GeneXpert phase
  • Answers must include input from all key stakeholders
  • Work by diverse groups need to be integrated

• Compiled in one place for any test developer to freely access

• More importantly, we need a ‘honest broker’ agency/team to:
  • help answer more nuanced questions
  • technical assistance with product development and validation
  • make the connections that test developers want
Thank you!

• To the NDWG for this opportunity

• To all companies, test developers and colleagues who provided input

• Additional comments are welcome!
  
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Disclosure

• No financial/industry conflicts
• I have co-chaired the NDWG in the past
• I currently serve as a consultant to the Bill & Melinda Gates Foundation (but my talk reflects my personal views)
• I receive grant support from the Bill & Melinda Gates Foundation, CIHR & Grand Challenges Canada