Regulatory needs and business case for ensuring product sustainability

March 23, 2017

Marco Schito (C-Path)
Madhukar Pai (McGill)
Jim Gallarda (Bill & Melinda Gates Foundation)
VISION FOR RDST

Global Data Contributions

Geno/Pheno/Clinical

Rapid DST Consortium

Use Cases
- Research
- Surveillance
- Clinical
- Diagnostic
  - WGS (centralized)
  - Targeted NGS (personal)
  - Probe-based (POC)
  - Culture-based (confirm)

Standards

Policy
Neglected Diseases, Delinquent Diagnostics

Diagnostic tests constitute 3 to 5% of health care spending but influence ~70% of health care decisions (1). Furthermore, less than 5% of annual spending on R&D is allocated to diagnostics for neglected diseases (2)—tropical infections common in underdeveloped countries, such as malaria, leishmaniasis, and tuberculosis (TB) (3).

Last month, the United States and 26 other countries commenced an effort—the Global Health Security Agenda—to prevent and address infectious disease outbreaks before they can spread around the world (4). The effort will focus on improving disease monitoring and developing tests for various pathogens. Although the initiative recognizes the need for new diagnostics, the expenditures for the entire effort are hardly sufficient for the extensive undertaking ($40 million this year from the U.S. Centers for Disease Control and the U.S. Department of Defense and $45 million being sought for next year).
GLOBAL CONCERN OVER AMR

No antibiotics without a test, says report on rising antimicrobial resistance

Report by economist Jim O’Neill says global cost of problem could be loss of 10 million lives a year by 2050 and $100tn a year

PRODUCT DEVELOPMENT IS STALLED FOR MANY GLOBAL HEALTH DIAGNOSTICS

Diagnostic landscape reports for global diseases
• Insufficient investment (money, time)
• Academics and funders are risk-averse
• Inadequate public-private partnerships
• Market forces and decisions
• Regulatory hurdles

End result
1. Likelihood of getting a product across the finish line is low
2. Larger diagnostic companies buy out the small number of successful entrepreneurs
THE IDEAL: SINGLE, LINEAR VALUE CHAIN
In reality, several intersecting* value chains...

- Product development value chain
- Product evaluation value chain (clinical trials and evidence)
- Policy value chain (global and country-specific)
- Implementation value chain (scale up)
- Impact assessment value chain

- All have different stakeholder groups with different agenda and goals

*often, these value chains do not intersect and that is a problem!
THE REAL: FRAGMENTED VALUE CHAIN

Poor understanding of pathogenesis and lack of suitable markers

Fragmented, lengthy and costly premarket approval processes

Lack of systematic evaluation processes

Need

Target/biomarker

Prototype

Lab & field evaluation

Regulatory approval

Technology assessment

Sales

Product profile

Test platform

Sample collection

Mid volume production

Scaled-up production

Distribution network & maintenance

Usage

Sales

Lack of gold standard

Lack of regulatory oversight

- Multi-country approval lengthy

- Process not well defined

Developers operate on high-volume low markup

Fragmented Market
- POC, triage, monitoring...
- Environmental conditions
- Market forecast and size?

Poorly defined market and unclear technical product profiles

Access to well validated samples

Access to finance

Access to P3 lab facilities

Cost and delay of clinical performance studies

McNerney, Diagnostics 2015
**But, If We Want To Solve A Problem, We Can!**

- 80 companies in development & 11 commercial Dx with authorization by FDA or WHO

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Manufacturer Sensitivity</th>
<th>Manufacturer Specificity</th>
<th>Independent verification</th>
<th>Targets</th>
<th>Additional materials</th>
<th>Time to results (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA and WHO EUA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ReEBOV</td>
<td>Corgenix</td>
<td>92%*2</td>
<td>85%*2</td>
<td>LoD verified, performance field-tested</td>
<td>ZEBOV</td>
<td>3</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Xpert Ebola</td>
<td>Cepheid</td>
<td>90-100%</td>
<td>100%</td>
<td>LoD verified</td>
<td>ZEBOV</td>
<td>6</td>
<td>1.5</td>
</tr>
<tr>
<td><strong>WHO EUA only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liferiver</td>
<td>Shanghai BioTech</td>
<td>Label unavailable</td>
<td>Label unavailable</td>
<td>LoD verified</td>
<td>ZEBOV + 3 other EV</td>
<td>10</td>
<td>4-6 or less</td>
</tr>
<tr>
<td>RealStar Filovirus</td>
<td>Altona</td>
<td>100%*5</td>
<td>100%*5</td>
<td>Performance verified</td>
<td>ZEBOV + 4 other EV</td>
<td>12</td>
<td>4-6 or less</td>
</tr>
<tr>
<td><strong>FDA EUA only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RealStar Ebolavirus</td>
<td>Altona</td>
<td>100%</td>
<td>100%</td>
<td>None</td>
<td>ZEBOV + 4 other EV</td>
<td>12</td>
<td>4-6 or less</td>
</tr>
<tr>
<td>BioThreat-E</td>
<td>BioFire</td>
<td>96%</td>
<td>100%</td>
<td>None</td>
<td>ZEBOV</td>
<td>5</td>
<td>1.25</td>
</tr>
<tr>
<td>NGDS BT-E</td>
<td>BioFire</td>
<td>87-92%</td>
<td>100%</td>
<td>None</td>
<td>ZEBOV</td>
<td>5</td>
<td>1.25</td>
</tr>
<tr>
<td>LightMix</td>
<td>Roche</td>
<td>98%</td>
<td>100%</td>
<td>None</td>
<td>ZEBOV</td>
<td>18*</td>
<td>4-6</td>
</tr>
<tr>
<td>EZ1</td>
<td>US DoD</td>
<td>100%</td>
<td>100%</td>
<td>None</td>
<td>ZEBOV</td>
<td>14</td>
<td>4-6</td>
</tr>
<tr>
<td>CDC NP</td>
<td>CDC</td>
<td>98-100%</td>
<td>100%</td>
<td>None</td>
<td>ZEBOV</td>
<td>24</td>
<td>4-6</td>
</tr>
<tr>
<td>CDC VP40</td>
<td>CDC</td>
<td>100%</td>
<td>94-100%</td>
<td>None</td>
<td>ZEBOV</td>
<td>24</td>
<td>4-6</td>
</tr>
</tbody>
</table>

**Strength of product:**
- High
- Medium
- Low

**Technology:**
- PCR
- Antigen detection

1 Results from manufacturer-reported contrived clinical specimen studies; 2 Results from WHO clinical evaluation vs. RealStar; 3 Sensitivity and specificity; 4 Number of instruments, reagents, and other materials required but not provided; 5 Based on analytic studies; 6 Automatic nucleic acid extraction

Source: WHO Selection Of IVD Guidance June 2015, FDA Emergency Use authorizations, Device labels

Slide courtesy: Jim Gallarda, BMGF
Even when tests exist, empirical RX is widespread

Use of standardised patients to assess quality of tuberculosis care: a pilot, cross-sectional study

Summary
Background Existing studies of the quality of tuberculosis care have relied on recall-based patient surveys, questionnaire surveys of knowledge, and prescription or medical record analysis, and the results mostly show the health-care provider’s knowledge rather than actual practice. No study has used standardised patients to assess clinical practice. Therefore we aimed to assess quality of care for tuberculosis using such patients.

Compounding diagnostic delays: a qualitative study of point-of-care testing in South Africa

Barriers to Point-of-Care Testing in India: Results from Qualitative Research across Different Settings, Users and Major Diseases

Treatment as diagnosis and diagnosis as treatment: empirical management of presumptive tuberculosis in India

‘Multiple-test’ approach to the laboratory diagnosis of tuberculosis - perception of medical doctors from Ujjain, India

Slide courtesy: Madhukar Pai (McGill)
Scale up has often dragged on for diseases in LMIC

While drugs, diagnostics, and vaccines typically scale within the first two years of launch in developed countries, they often take decades to scale in lower- and middle-income countries.

Source: Bill & Melinda Gates Foundation
ADDITIONAL DIAGNOSTIC IMPLEMENTATION CHALLENGES

• Reducing diagnostic value chain fragmentation
• Defining diagnostic approval process
• Strengthening linkage to care and treatment
• Health care system strengthening (including connectivity)
• Supply chain management
• Adoption of country policy to address local challenges (algorithms)
• Maintenance and repair
• Training and retention
LOOK AHEAD AT TODAY’S SESSIONS

1. Regulatory and policy: shape country policy and drive markets
   – Current thinking from FDA, EUCAST and WHO around use of NGS for TB
   – Panel discussion including thoughts from industry leaders

2. What is the business case for developing IVD for addressing diseases of global health importance?
   – Models for addressing sustainability
   – Viewpoints from developers

3. Closing Remarks
UK Genomic Analysis Firm Congenica Raises $10M
Feb 27, 2017 | staff reporter

NEW YORK (GenomeWeb) – Congenica announced today that it has raised £8 million ($10 million) after closing a round of Series B financing.

The British genomics company will use the proceeds from the round to accelerate marketing efforts for its Sapientia clinical genome analysis platform.

CEO Tom Weaver said in a statement that the funds should enable Congenica to “establish us as an ‘international leader in data solutions’ for diagnosis of rare genetic diseases and allow Congenica to ‘realize the next steps in product development’ and in supporting [its] growing user base,” he said.

Congenica Eyes US, Chinese Markets, Plans Product Upgrades Following $10M Financing Round
Feb 27, 2017 | Justin Petrone

NEW YORK (GenomeWeb) – Congenica, a Cambridge, UK-based genomic analysis company, announced this week that it has closed a £8 million ($10 million) round of Series B financing that it will use to build its commercial operations and further develop its product.

CEO Tom Weaver and COO Nick Lench said in interviews that the company will use the proceeds to establish its presence in the US and China, where it will court not only clinical genetics laboratories, but specialists, academics, and biotechnology and pharmaceutical firms as potential customers for its flagship Sapientia genome analysis platform.