The Challenges Along the Pediatric Diagnostics Continuum: Development and Implementation

Maurine M. Murtagh
Thematic Roundtable on Paediatric HIV Diagnostics: Early Infant Diagnosis and Beyond
Industry Liaison Forum/IAS/CIPHER
19 July 2015
The road from discovery to delivery of diagnostic products involves many steps.

And the process can easily take 5 years or more, even after prototype development, and can cost from $5 million to $50 million or more.
The Obstacles to Product Development – Product Needs

One of the first challenges for product developers is to know what diagnostic(s) is/are needed in the market and for use in which settings.

For some diagnostics, including for EID for use at the point-of-care (POC), there are Target Product Profiles available to provide guidance. But, even with such guidance, the market for a given assay will grow or diminish due to changes in guidelines and other factors.

For example, with new WHO guidance in 2013 on viral load testing for monitoring patients on ART, the market for CD4 testing is being diminished.

The result has been the failure of some POC CD4 assays to reach the market for lack of funding.
Once a developer has targeted an assay for development, early obstacles often include *technology issues* – i.e., the performance of the test device is inadequate. In the worst case, the developer may have to go back to the drawing board to redesign the product, which can cost months or more in the timeline.

In addition, *funding* is frequently an early barrier to product development and can slow the process.

Mobilizing funding for diagnostic products designed for the developing world is particularly difficult because financial returns on the product are generally expected to be low.
The Obstacles to Product Development - Funding

Discovery
- Basic Research
- Platform development and feasibility studies

Proof of Principle
- Prototype development
- Clinical Trials

Product Development
- Product Optimization
- Pre-market Validation
- Scale-up/Manufacturing

Delivery
- Commercial release and Marketing

Funding Sources:
- NSF, NIH, NIAID, BMGF, Corporate R&D, SBIR Phase I
- Angel investors, Corporations, Technology labs, SBIR Phase II
- Venture capital
- Corporate venture funds, equity, commercial debt

Valley of Death

Source frequently funds this technological stage
Source occasionally funds this technological stage
Challenges of Product Launch

• Once financial and technical hurdles have been overcome and prototype development/proof of concept are achieved, the developer can refine and target the use of the product based on the results of early evaluations (pre-market validation).

• After completing these, all diagnostics must undergo laboratory evaluations to assess their analytical performance compared to reference assays.

• Developers also need to seek regulatory approvals for assays – e.g., pre-qualification.

• Manufacturing facilities must be set up and distribution partners must be identified.
In-Country Product Introduction – Regulatory Approval

Generally speaking, there are complex, non-uniform and costly regulatory frameworks for evaluation and registration of new products at the national level in-country.

Even with PQ and other regulatory approvals (e.g., CE-IVD), evaluation of the product’s clinical performance in field settings will generally be required. These trials are costly to the developer and often have to be done in most, if not all, of the countries in which the company wishes to sell its diagnostic.

These trials are one of the last major hurdles in product development, followed by final scale-up of production and commercial marketing of the new diagnostic.
Paving the Way from Product Development to Approval

• Extensive fundraising will generally be necessary, and there are few ways to short-cut this step.

• Technical issues are almost bound to arise and must be dealt with by the development staff.

• There are efforts underway by many partners, including regional regulatory organizations like the PAHWP, international organizations like WHO PQ, and others, including LSHTM, to streamline and harmonize regulatory requirements. It is a slow process.
Once a product has approval in-country and is registered, there are still obstacles and barriers to smooth product uptake and implementation. These include:

- Strategic planning
- Budgeting/procurement
- HR and Training
- Quality Assurance
- Service and Maintenance
- Supply chain/Data management
How to Deploy the Technology – Strategic Plans for POC

• With the experience of implementing POC CD4, countries have learned many lessons and are better prepared to implement POC EID and viral load testing.

• Many countries have developed strategic plans for implementing POC diagnostics. This should help to smooth implementation.

• But countries can still use guidance from partners with respect to the characteristics of POC diagnostics in order to make strategic decisions about product placement and product choice.

• Without this, procurement and deployment in-country is piecemeal, which can be fatal to suppliers, especially if they are smaller companies.
Budgetary/Procurement Issues

• Increasing the in-country diagnostic budget to include a new technology can be problematic.

• Diagnostic procurement budgets (both for governments and NGOs) are generally set a year or more in advance, and registration of a new diagnostic may not fall in line with the budget cycle.

• The result is that funding for procurement of a new diagnostic may have to wait before it can be included in the budget and before substantive funds are available.

• This can also lead to gaps in procurement.
Training is particularly difficult to do with POC assays because training health care workers on a large scale is generally required; this generally exacerbates HR capacity shortages.

But, without appropriate training, POC test results are likely to be inaccurate.

Given chronic staff turnover in most sites, training must be repeated.

Training of trainers and other approaches are required.

Mentoring is an effective strategy.
Quality Assurance

- Monitoring the quality of tests and testing is more difficult as testing is decentralized – with more operators performing tests at many more sites.
- The experience of POC testing has demonstrated that poor quality often results, even with the simplest of tests.

- To address this, countries are designing national QA programs for POCT.
- EQA providers are working with countries to help provide panels for testing.
Service and Maintenance

- Instruments are often out of service, especially outside of central reference facilities.
- Outages can often extend for months or longer.
- Service and maintenance agreements negotiated at time of platform purchase.
- For POC devices: No annually scheduled preventive maintenance required; instrument has capability to send an alert or to be detected remotely when it is not functioning properly.
- Mean time to failure: >12 months.
Supply Chain/Data Management: Connectivity

- Transport of supplies is slow and roads are poor; can easily take 8 hours by surface transportation to travel 150 miles in some countries.
- Stock-outs of kits and reagents are exacerbated by poor ordering and inventory management.
- Test results are transcribed in logbooks at the end of the day; then added to patient record.
- Missing data (no dates, results, etc.); no common patient IDs.
Supply Chain/Data Management: Connectivity

• Employing connectivity solutions for diagnostic platforms can be a way to improve both lab systems and diagnostic access.
• There is a need to capture data (patient IDs, lot number of cartridges, etc., coordinates of location).
• There is also a need to export data wirelessly with user-initiated export; and to have data pull capabilities, if necessary.
• And, there is a need to manage data for QA and surveillance purposes.
Where does that leave us?
Some Ways to Help Pave the Way

• **Ongoing in-country capacity building to improve diagnostic systems.**

• Strong, coordinated efforts by stakeholders to **harmonize regulatory requirements** across countries and to streamline **evaluations of new diagnostic platforms**. These efforts are already underway.

• **Targeted technical assistance on the adoption of new technology**, focusing on selection of new diagnostic technologies, procurement planning and budgeting, coordination of partners around a national budget and implementation plan.

• **Clear, objective information** on consensus-driven product standards; accredited in-country evaluation sites; regulatory landscapes and issues; quality assurance systems.

• **Practical tools** to determine strategic placement of new IVD technologies and **models** for estimating cost-effectiveness and impact of such technologies.
Thank you