Stimulating introduction of new, innovative in vitro diagnostics

Supporting product development

Gonzalo Domingo
Diagnostics
gdomingo@path.org
09/18/2017
PATH: Accelerating global health innovation

- 40 YEARS OF EXPERIENCE
- 94 PRODUCTS IN THE PIPELINE
- FROM R&D TO SCALE-UP: FOCUSING ON "MIDDLE OF THE VALUE CHAIN" WHERE GREATEST CHALLENGES LIE
- 70 COUNTRIES
- AVERAGE OF 150 MILLION PEOPLE SERVED PER YEAR
- EXPERTISE IN 5 PLATFORMS
- SERVING WOMEN AND CHILDREN
- WWW.PATH.ORG

TECHNOLOGIES

2014 2015 2016 2017 2018

40 YEARS OF EXPERIENCE
94 PRODUCTS IN THE PIPELINE
Contents

1. Case study: Malaria diagnostics
   - Case management
   - Malaria elimination

2. Current situation:
   - Challenges and opportunities and recent developments

3. Summary
Case study: malaria diagnostics

- Malaria case management
  - Need: point-of-care diagnostics for G6PD deficiency to inform treatment of *Plasmodium vivax* malaria
Case study: malaria diagnostics

• Malaria case management
  • Need: point-of-care diagnostics for G6PD deficiency to inform treatment of *Plasmodium vivax* malaria

• More sensitive diagnostic tests for malaria to support malaria elimination
  • Need: point-of-care tests that detect the asymptomatic malaria parasite reservoir
Universal access to treatment. Curing *P. vivax* malaria

1. *P. vivax* malaria comes back after treatment with typical antimalarial drugs

   - Primary attack may be absent

2. Curing a patient requires special drugs to kill the parasites in the liver

   - Primaquine (14 day regimen)
   - 8-aminoquinoline
   - Tafenoquine (single dose regimen)

3. Current options for curing a patient of *P. vivax* malaria present a risk of acute red blood cell lysis in patients with G6PD deficiency: a common human genetic disorder

Hankey DD, et al., 1953, Korean vivax malaria. I. Natural history and response to chloroquine
G6PD activity: Spectrophotometric quantitative test

POC-G6PD test

Hb-normalized G6PD (IU/g Hb)

Hemoglobin (g/dL Hb)

Hemoglobin reader

Hemocue disposables

G6PD kit

uv cuvette

controls

uv spectrophotometer (thermo-regulated)

Universal access to treatment. Curing *P. vivax* malaria
Detecting the malaria parasite reservoir to support malaria elimination

Current tests

Ultra-sensitive PCR

Parasites per µl blood

Number of Asymptomatic People
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Current situation: challenges and opportunities
Concept, risk analysis and value proposition assessment

### Phase 1: Concept and risk analysis

### Phase 2: Design and verification

### Phase 3: Validation

### Phase 4: Registration & Launch

### Phase 5: Post launch assessment

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**Technical Specifications Series**

[TSS-2] Technical specifications for WHO prequalification of Glucose-6-phosphate dehydrogenase (G6PD) in vitro diagnostics (IVDs)

[Draft] Technical specifications for WHO prequalification of Glucose-6-phosphate dehydrogenase (G6PD) in vitro diagnostics (IVDs)
Current situation: challenges and opportunities
Concept, risk analysis and value proposition assessment

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Challenges | Opportunities
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Pro-active stakeholder engagement in product specifications development

Inadequate and evolving regulatory landscape | 2. ENSURING QUALITY
Regulatory harmonization initiatives
Pre-emptive WHO PQ guidance and coordination with programs

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G6PD Prequalification: Public Announcement to Stakeholders

Type of Assessment
Products intended for G6PD testing in view of treatment with 8-aminoquinoline will be classified as Class C IVDs as per GFIT risk classification ... Class C IVDs are defined as IVDs presenting a high risk to the individual patient with a moderate public health risk. Furthermore, G6PD assays are currently regulated as low risk IVDs given that currently available assays are not specifically intended to guide clinical decision making on administration or withholding of anti-malarial treatment for radical cure of P. vivax. Consequently, all products submitted for WHO prequalification will undergo a full prequalification assessment.

Announcement: 15th April 2016
Current situation: challenges and opportunities
Concept, risk analysis and value proposition assessment

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| Pricing sensitivity and unrealistic target pricing | 3. SUSTAINABLE PRICING  
Increased awareness of pricing models for sustainable supply  
Increased pricing transparency |

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### RDT sales to NMCPs, 2010–2015

*Source: Manufacturer reporting to the WHO, World Malaria Report 2016*
### Current situation: challenges and opportunities

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<td><strong>Fragmented and unpredictable markets leading to poor resolution of market sizes</strong></td>
<td>Increasing experience and intelligence with realistic market sizing, demand forecasting and coordination of financing resources</td>
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#### Estimated market size for G6PD testing

Based on *P. vivax* case management needs per health care facility
Current situation: challenges and opportunities
Design and verification

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### Challenges

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<td>Unavailability of essential biologics, specimens and resources</td>
<td>Development of specimen panels, and relevant biologics are a recognized need by the not-for-profit sector</td>
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Malaria specimen panels
Malaria HRP2 recombinant panels
Malaria Standardized culture panels

G6PD specimen panel
Current situation: challenges and opportunities
Design and verification

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### Challenges

- Poor definition of product specifications
- Poor definition of success criteria and reference standards
- Unavailability of essential biologics, specimens, and resources
- Broad operating environment demanding stringent ruggedness testing
- Broad end-user profiles, from highly skilled to community health workers

### Opportunities

- Pro-active stakeholder engagement in product specifications development
- Development of international controls and standards are a recognized need by the not-for-profit sector
- Development of specimen panels, and relevant biologics are a recognized need by the not-for-profit sector
Current situation: challenges and opportunities

Validation

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**Challenges**
- Absence of clinical sites with adequate skills in target/endemic settings
- Unclear expectations for validation

**Opportunities**
- Clinical trial networks have improved significantly in the last 2 decades
- Improved intended use, and regulatory guidance

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[Draft] Technical specifications for WHO prequalification of Glucose-6-phosphate dehydrogenase (G6PD) in vitro diagnostics (IVDs)

**World Health Organization**

**Technical Specifications Series**

**TSS-2**
### Current situation: challenges and opportunities

#### Registration and launch

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#### Challenges

- Fragmented or absent regulatory oversight undermining investment in quality products
- Very fragmented and inconsistent registration requirements leading to unpredictable registration resource requirements and timelines
- Poor market intelligence and minimal market development to inform a demand driven registration strategy

#### Opportunities

- Improving regulatory oversight
- Regulatory harmonization initiatives
- Pre-emptive standard setting by WHO-PQ.
- Regulatory harmonization initiatives
- Essential diagnostics
- Global procurers
- Global programs

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Asian Harmonization Working Party (AHWP),
the Latin American IVD Association (ALADDIV)
the Pan African Harmonisation Working Party
Case study: POC tests for G6PD deficiency to inform malaria case management

After >20 years of no innovation in this space, the intended use for malaria case management in LMIC countries has driven the development of a robust pipeline for POC G6PD tests.
Case study: malaria elimination

Through innovation in biologics, materials and chemistry a new rapid diagnostic test with an order of magnitude improvement in limit-of-detection has been developed. This test detects a higher proportion of sub-microscopic malaria infections.
Summary

- There are many challenges to addressing diagnostic needs for LIMC
- WHO, donors and not-for-profit organizations recognize these challenges and are increasingly coordinating to risk mitigate these challenges through
  - Early clear definition of needs
  - Reference standards and quality guidance
  - Driving regulatory harmonization
  - Establishing biologic and specimen panels as common resources
  - Providing more realistic market estimates
- With the increasing overlap between LIMC markets and HIC markets, addressing diagnostic needs for LIMC represents a market entry opportunity
  - As observed by robust product pipelines targeting predominantly LIMC diagnostic needs
THANK YOU!

Donors