Update on Regional Harmonization of Diagnostic Regulation in Africa

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POC Diagnostics Initiative

• Develop an open point of care instrument platform capable of delivering optimum performance

• Establish interoperability standards to encourage menu expansion by competing companies/sources

• Reduce barriers to entry into global health markets by eliminating the need for expensive instrument development

• Achieve a harmonized regulatory environment
Regulation of In-vitro Diagnostics: Top 5 Challenges

1. Regulatory landscape for IVDs highly variable
2. Assessment of safety and quality based on risk classification but often lack rigour
3. The process of approval is not transparent
4. Approval is often costly and lengthy, especially for imported tests
5. Limited success with standardisation and harmonization

<table>
<thead>
<tr>
<th>GHTF Classification</th>
<th>Personal health risk</th>
<th>Public Health Risk</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class A</td>
<td>Low</td>
<td>Low</td>
<td>Stains, culture media</td>
</tr>
<tr>
<td>Class B</td>
<td>Moderate</td>
<td>Low</td>
<td>pregnancy tests</td>
</tr>
<tr>
<td>Class C</td>
<td>High</td>
<td>Moderate</td>
<td>Tests for TB</td>
</tr>
<tr>
<td>Class D</td>
<td>High</td>
<td>High</td>
<td>Blood screening tests, HIV</td>
</tr>
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Need for Regulatory Standards and Harmonization

• Tests are sold and used in much of the developing world without evidence of effectiveness

• Duplication in clinical performance studies and manufacturing inspections pose major barriers to market entry, resulting in delay in access and unaffordable pricing

• Companies with quality tests unable or unwilling to compete in market flooded with low quality tests

• Companies often do not bother marketing in countries with small markets
# Regulation of in-vitro Diagnostics

<table>
<thead>
<tr>
<th></th>
<th>Burundi</th>
<th>Kenya</th>
<th>Rwanda</th>
<th>Tanzania</th>
<th>Tanzania Zanzibar</th>
<th>Uganda</th>
<th>Ethiopia</th>
<th>Nigeria</th>
<th>South Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legal Framework</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>IVD regulated?</td>
<td>-</td>
<td>✓</td>
<td>-</td>
<td>✓</td>
<td>✓</td>
<td>-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

## Premarket Controls

| Risk Based classification | - | - | - | GHTF | GHTF | - | GHTF | In process | GHTF |
| Registration             | - | ± | - | ✓   | -   | - | ✓     | ✓        | ✓   |
| Clinical studies         | - | ± | - | Some ✓ | - | HIV | Limited | -       | ✓   |
| Evaluation capacity      | Limited KEMRI | Limited KEMRI | Limited | Some ✓ | - | HIV | Limited | -       | ✓   |

## Marketing Controls

| Advertising control      | ✓ | ± | - | ✓ | - | ✓ | ✓ | ✓ | ✓ |
| Market ing controls      | - | ± | HIV, TB | ✓ | - | ✓ | ✓ | ✓ | ✓ |

## Post-marketing Controls

| Surveillance             | - | ± | - | ✓ | - | - | - | - | ✓ |
| Lab accreditation        | - | ✓ | - | ✓ | - | ✓ | ✓ | - | ✓ |
| Device reporting         | - | ± | - | - | - | - | - | - | ✓ |
| Corrections/Recall        | - | ± | - | - | - | - | - | - | ✓ |
UNITAID LSHTM Project Goals and Outputs

Goal: Increase the availability and affordability of quality-assured HIV monitoring technologies and early infant diagnosis in resource-limited settings

**Diagnostic Targets**

**Technology Platform**

- **Product Prototype**
- **Proof of Principle**
- **Lab & Field Evaluations**
- **Policy and Guidelines for Use**
- **Test Adoption**

**Output 1:** A set product standards/target product profiles and standardised evaluation protocols

**Output 2:** A network of evaluation sites pre-approved for using standardised protocols; trial quality monitored

**Output 3:** Acceleration of policy development for point-of-care (POC) tests

**Output 4:** A national system of quality assurance for POC tests
Pan-African Harmonization Working Party

Founded in 2012 to steer regulatory harmonization activities in the region in partnership with AHWP, the Latin American Diagnostic Association and WHO

Founding members:
- African Union – New Partnership for Africa’s Development (AU-NEPAD)
- East African Community (EAC)
- African Society for Laboratory Medicine (ASLM)
- GIZ
- LSHTM

PAHWP Advisory Group (under the African Advisory Group for Regulatory Harmonization of Medicines, Medical Devices and Diagnostics, AU):

Chair: EAC
Vice-Chair: Nigeria
Secretary: South Africa

Technical Working Groups:
1. Risk Classification
2. Common Registration File
3. Convergence on inspections of manufacturing sites
4. Reduction in number of clinical trials
5. Post-marketing surveillance

First African Regulatory Forum for Medical Diagnostics held on July 24-26 2013 in Nairobi, Kenya
# Five Priority Focus Areas for Regulatory Harmonization for PAHWP and their Impact

<table>
<thead>
<tr>
<th>Regulation</th>
<th>Harmonization Priorities</th>
<th>Results</th>
<th>Impact</th>
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</thead>
<tbody>
<tr>
<td>Risk Classification</td>
<td>A common risk classification system – adoption of the GHTF system</td>
<td>• More streamlined regulatory process</td>
<td>• More affordable IVDs</td>
</tr>
<tr>
<td>Registration File</td>
<td>A common dossier template – Adoption of the WHO PQ dossier</td>
<td>• Duplication in clinical performance studies and audits reduced</td>
<td>• Faster access to quality-assured diagnostics</td>
</tr>
<tr>
<td>Clinical Performance Studies</td>
<td>A network of evaluation sites pre-approved by IRBs to use standardised protocols Joint review of data from evaluations</td>
<td>• Companies save time and money</td>
<td>• Better patient outcomes</td>
</tr>
<tr>
<td>Quality System Audits</td>
<td>Convergence of standards and 3rd party recognition of audits (MDSAP)</td>
<td>• Assurance of diagnostic quality</td>
<td>• Supports innovation</td>
</tr>
<tr>
<td>Post-Marketing Surveillance</td>
<td>Regional laboratory networks to monitor test quality</td>
<td>• Assurance of diagnostic quality</td>
<td>• More public confidence in diagnosis</td>
</tr>
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Common Registration File

- Use POC tests for CD4, HIV viral load and early infant diagnosis to pilot a Common Registration File

- Training: compile elements of:
  - Good Review Practice for regulators
  - Good Submission Practice for industry

PQ Application:
1. Manufacturer Information
2. Product Information
3. Product disease category, analyte and method
4. Product Operation
5. Product Performance
6. Product – Commercial and Regulatory Status
7. Manufacturer QMS
8. Manufacturer ISO 13485:2003 Certification
9. Site of product manufacture
10. Manufacturer Declaration
Training for Joint Review of Clinical Performance data from HIV POC Test Evaluations in 2014

Faculty:
WHO PQ
Regulatory consultant
LSHTM

Creation of Virtual Campus
• e-learning materials
• mentoring online
• face to face workshops
PAHWP is hosted within the African Union-NEPAD Planning and Coordinating Agency

May 13 2014: EAC approved 3 antimalarials & 2 health products
Collaboration and information sharing among countries in Southern Africa is key in meeting the mandate of providing access to safe, affordable, quality medicines.

National Medicines Regulatory Authorities in Zambia, Zimbabwe, Botswana and Namibia, with support from WHO-PQT have formed the Zazibona initiative and undertaken ongoing pilot collaborative activities.

The 4 countries share several commonalities and face similar challenges regarding medicine regulations which create an opportunity for a mutually beneficial collaboration. The benefits include:
• reduction of regulatory workload
• accelerated registrations of required products
• mutual trust and confidence in regulatory collaboration
• improved information sharing and networking
Grand Challenges Canada: Progress towards IVD Regulatory Harmonization 2012-14

Asia Harmonization Working Party (23 countries). IVD sub group

Latin America Diagnostic Association (ALADDIV) (12 countries)

Pan-African Harmonization Working Party (23 countries)

15 member states in SADC: Angola, Botswana, DRC, Lesotho, Malawi, Mauritius, Mozambique Namibia, Seychelles, South Africa Swaziland, Tanzania, Zambia Zimbabwe, Madagascar

Ghana, Sierra Leone
Summary

• Regulation ensures the quality, safety and effectiveness of diagnostics to improve health outcomes

• The Pan-African Harmonization Working Party (PAHWP) has been created within the African Union NEPAD agency to strengthen regulatory oversight through harmonized approaches

• LSHTM through funding from UNITAID is committed to working with WHO, UNICEF, AU-NEPAD, PAHWP, ASLM and other partners to streamline and accelerate the evaluations and review of new HIV POC tests.

• Ongoing support to the AU NEPAD agency, PAHWP and regional economic communities is key to improving the regulatory oversight of diagnostics in Africa