Moving towards Regulatory Harmonization of *in-vitro* Diagnostics: update from Latin America

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London School of Hygiene & Tropical Medicine  
United Kingdom
Regulatory Harmonization for IVDs

- Regulation of IVDs: Top 10 challenges
- Why harmonization and why now?
- Overall programme goal and priorities
- The IVD initiative in Latin America: ALADDIV
- Inter-regional collaboration
- Moving forward
Diagnostics Bench to Bedside Pathway

Product Development
- Diagnostic Target Discovery
- Platform development
- Prototype & Proof of Principle
- Pre-market Validation

Product Evaluation
- Lab evaluation
- Field evaluation
- Lab evaluation → Analytical Performance
- Field evaluation → Clinical Performance
- Regulatory Approval

Marketing
- Policy & Implementation

10-12 years
2-5 years
5-7 years
Regulation of In-vitro Diagnostics: Top 10 Challenges

1. Regulatory landscape highly variable
2. Regulatory approval processes lengthy, especially for imported tests
3. Most approval processes not transparent
4. Reviews often lack quality standards
5. Clinical performance studies often not required or lack rigour
6. Tests are sold and used in the developing world without evidence of effectiveness
7. Cost of regulatory approval pass onto end-users
8. Companies with quality tests unable or unwilling to compete in market flooded with low quality tests
9. Limited success with standardisation and harmonization
10. Companies often do not bother filing in countries with small markets
Global Harmonization Task Force (GHTF)

- GHTF was conceived in 1992 in response to the growing need for international harmonization in the regulation of medical devices to ensure the safety, effectiveness and quality of medical devices.
- GHTF published and disseminated harmonized documents on basic regulatory practices and served as an information exchange forum. GHTF documents are developed by 5 Study Groups (SG):
  - SG1 - Premarket Evaluation
  - SG 2 - Post-Market Surveillance/Vigilance
  - SG 3 - Quality Systems
  - SG 4 - Auditing
  - SG 5 - Clinical Safety/Performance
- In 2012, GHTF transitioned to a purely regulatory body called the International Medical Devices Regulatory Forum (IMDRF) which will continue to promote the principles of harmonization.
Asia Harmonization Working Party (AHWP)

**Member Economies: (N=23)**
- Brunei, Cambodia, China, Hong Kong, India, Indonesia, Korea, Laos, Malaysia, Myanmar, Pakistan, Philippines, Singapore, Taiwan, Thailand, Vietnam
- Abu Dhabi, Chile, Jordan, Kuwait, Saudi Arabia, South Africa, Yemen

- The Chair of AHWP for 2012-14 is Dr. Saleh S. Al-Tayyar
- Six working groups:
  - Work Group 1 (WG1) - Pre-Market Submission and CSDT
  - Work Group 1a (WG1a) - IVDD
  - Work Group 2 (WG2) - Post-Market Surveillance and Vigilance
  - Work Group 3 (WG3) - Quality Management System
  - Work Group 4 (WG4) - Quality System Audit
  - Work Group 5 (WG5) - Clinical Safety/Performance
  - Work Group 6 (WG6) - Capacity Building and Regulatory Training
  - Special Task Group (STG - Nomenclature) - Medical Device Nomenclature
HIV/AIDS Global Targets

- Place 15 million people on ART by 2015
- Eliminate new HIV infections in children
- Intensify HIV prevention

As of 2012:
9 million HIV patients are on ART

Investments of at least US$22 billion are needed by 2015

United Nations General Assembly High Level Meeting on AIDS, 2011
Pipeline for POC Diagnostics

CD4 Product Pipeline*

*Estimated as of March 2013 - timeline and sequence may change.
HIV Viral Load Product Pipeline

- Alere Q
- EOSCAPE HIV™ Rapid RNA Assay System
- Wave 80 Biosciences
- Truelab PCR
- Molbio/bigTec
- Gene Xpert
- Gene-RADAR
- Nanobiosym

- SAMBA VL
- DDU/Cambridge
- Liat™ Analyser
- IQuum
- RT CPA HIV-1 Viral Load
- Ustar
- Viral Load Assay with BART
- Lumora

Regulatory Harmonization for in-vitro Diagnostics

**Goal:** faster access to affordable POC diagnostics

**Strategy:** define a regulatory pathway that is “better, faster, safer and cheaper”

**Technical Working Groups:**
1. Risk Classification
2. Common Registration File
3. Quality management audits of manufacturing sites
4. Clinical evidence
5. Post-marketing surveillance
Regulatory Oversight: Better, Safer, Faster & Cheaper

**Harmonization Activities**

**Pre-market Controls**
- review of risk based classification systems
- Adoption of a common classification system
- Create an AU-NEPAD classification panel

**Registration file**
- Consensus on essential data for review
- Adoption of a common registration file
- Training on Good Review Practice

**Clinical performance studies**
- Development of common protocol
- Establishment of trial ready sites
- Joint review of trial data

**Manufacturing site audits**
- Convergence of standards
- Mutual or 3rd party recognition of audit results (MDSAP)

**Marketing Controls**

**Post-marketing Surveillance**
- Establish regional lab network to monitor POCTs
- Develop system for reporting product failures
- Mechanism for corrective action/recalls

**Results**
- A common classification system
- A common submission template
- More country approvals for fewer trials
- Reduce duplication of audits

**Impact**
- More streamlined regulatory process supports innovation
- Companies saves time, effort and money
- More affordable IVDs
- Faster access of quality-assured diagnostics
- Better patient outcomes
- Ongoing assurance of quality of POCTs
- More public confidence in diagnosis
Harmonization in Latin America

• 18 of 41 countries in Latin America implement medical devices regulations: Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Ecuador, Guatemala, Honduras, Jamaica, Mexico, Nicaragua, Panama, Peru, Puerto Rico, Uruguay, Venezuela

• **UNASUR** (Unión de Naciones Suramericanas) (*N* = 12),
  - Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Guyana, Paraguay, Peru, Suriname, Uruguay, Venezuela,
  2 observers: Mexico, Panama
  
  UNASUR was constituted on May 23, 2008, at the Third Summit of Heads of State, with the Creation of a single market by merging CAN and Mercosur
  
  CAN: the Andean Community of Nations: Bolivia, Colombia, Ecuador, and Peru
  
  Mercosur: Argentina, Brazil, Paraguay, Uruguay, Venezuela

• **Goals:**
  - **Economic Development:** finance economic development projects to improve local competitiveness and to promote the scientific and technological development of the member states, and reduce asymmetries
  
  • **Infrastructure cooperation**
## Current Pathway for Approval of Medical Devices 1. Latin America

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# Regulation of in-vitro Diagnostics

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Advanced Course in Diagnostics
Annecy, France, Sept 2011
Creation of Latin America IVD Association: April 2012

- 80 participants from regulatory authorities, MOH, research institutes and laboratories from:
  - Argentina, Bolivia, Brazil, Colombia
  - Cuba, Guatemala, Paraguay, Peru, Uruguay, Venezuela, Mexico, Panama

Industry representation from 13 companies:

- Abbott, Alere, BioEasy, BioMerieux, BioRad, Diasorin, LabTest, Novociclo, OrangeLife, Roche, Sysmex, Thermofisher, WAMA diagnostics and diagnostic associations

Commitment for convergence of standards and pooling regulatory expertise
Organización Panamericana de la Salud

WORKSHOP
“Testes de Diagnóstico in Vitro Acessíveis e com Qualidade Assegurada para Programas de Saúde Pública”
17 e 18 de Abril de 2012 - Brasília/Brasil
The South American Institute of Government in Health (ISAGS)

• ISAGS is a public, intergovernmental entity within the South American Health Council of the Union of South American Nations (UNASUR); with permanent headquarters in Rio de Janeiro
## Influence of other approvals on Regulatory Approval in 17 countries in South America

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<th>Pre-requisite/Expedites</th>
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<td>EU CE Mark</td>
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<td>WHO/PQ &amp; Bulk Procurement</td>
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<td>USAID waiver list</td>
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<tr>
<td>CDC Evaluation</td>
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Countries included: Argentina, Bolivia, Brazil, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Uruguay
Priorities in the Region

• **Future Regulatory Framework in Americas**
  – UNASUR and the future of Health in South America (Coordinator of ISAGS)
  – Common Dossier Submission (ANVISA)
  – GMP and Quality Systems Audits
    – MERCOSUR countries (Argentina, Brazil, Praguay, Uruguay, Venezuela) have harmonised GMP inspections
    – Brazil is working with USFDA and Canada on MDSAP
  – Laboratory Networks
  – Post Marketing Surveillance

• **Quality Assurance and Assessment**
  – Analysis and Support to the Surveillance System
  – Post market surveillance
  – Network collaboration
  – Health Technology Assessment for IVDs – The Role of RedETSA (Network of Health Technology Assessment of the Americas initiated by Dr Christophe Rerat – PAHO)
## Inter-regional Regulatory Harmonization Activities

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tr>
<td><strong>2011:</strong></td>
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<tr>
<td>Sept.</td>
<td>South Africa IVD Directive Consultation</td>
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<tr>
<td>Nov.</td>
<td>AHWP 16th Annual meeting</td>
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<td><strong>2012:</strong></td>
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<td>Mar.</td>
<td>East African Community (EAC)</td>
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<td>Apr.</td>
<td>Latin American Association for IVDs workshop, PAHO, Brasilia</td>
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<tr>
<td>May</td>
<td>African Society for Laboratory Medicine &amp; AHWP workshop</td>
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<tr>
<td>July</td>
<td>EAC meeting to set up PAHWP</td>
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<tr>
<td>Nov.</td>
<td>Latin American Association for IVDs workshop, ANVISA, Brasilia</td>
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<tr>
<td>Dec.</td>
<td>AHWP 17th annual meeting &amp; PAHWP launch at ASLM Conference</td>
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<tr>
<td><strong>2013:</strong></td>
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<tr>
<td>May.</td>
<td>AHWP WG1a workshop</td>
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<td>July.</td>
<td>First African Regulatory Forum for Medical Diagnostics, Nairobi</td>
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<tr>
<td>Sep.</td>
<td>Inter-regional workshop convened by AHWP</td>
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<tr>
<td>Oct.</td>
<td>Latin American Association for IVDs, Curitiba, Brazil</td>
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<tr>
<td>Nov.</td>
<td>ISO TC 212: ISO standard for IVD clinical performance studies</td>
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<tr>
<td>Dec.</td>
<td>AHWP 17th annual meeting</td>
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Grand Challenges Canada: Progress towards IVD Regulatory Harmonization 2011-13

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

Latin America Diagnostic Association (ALADDIV) (12 countries)

Pan-African Harmonization Working Party (20 countries)

15 member states in SADC: Angola, Botswana, DRC, Lesotho, Malawi, Mauritius, Mozambique Namibia, Seychelles, South Africa Swaziland, Tanzania, Zambia Zimbabwe (Madagascar)
Moving Forward: least burdensome approach to:

- Reduce Costs
- Faster Access
- Save Lives
- Support Innovation
Moving Forward

• Inter-regional collaboration on regulatory harmonization:
  - Mar 2014: AHWP/ALADDIV workshops
  - Mar 2014: IMDRF on medical device single audit programme (MDSAP)
  - Jul 2014: 3rd African Regulatory Forum on Medical Diagnostics

• Need to create new models of public-private collaboration to:
  - support innovation
  - create an enabling environment for accelerating market entry and patient access to quality-assured diagnostics

• Need to build regulatory capacity in countries within the context of harmonization and efficiency

• Need to brainstorm on how regulatory science can keep pace with technological advances
Thank you

- LSHTM: Ruth McNerney, Kim Sollis, Rhosyn Tuta, Beth Downe
- AU: Paul Tanui
- EAC: Stanley Sonoiyia, Jane Masingia, Louisa Kosimbei
- WHO: Jean-Bosco Ndihokubwayo, Willie Urassa, Robyn Meurant
- ASLM: Trevor Peter, Tsehaynesh Messele
- GIZ: Wesley Ronoh, Thomas Walter
- PAHWP: Issac Kadowa, Ilonze Chinyere, Sagie Pillay, Sarvashi Moodliar, Patience Dabula, Agnes Kijo
- AHWP: Liling Liu, Albert Poon, Jeffrey Chern, Jack Wong, Benny Ons
- ALADDIV: Carlos Gouvea, Adele Benzaken, and many others
- National regulatory authority representatives
- Consultants: Maurine Murtagh, Ben Cheng, Elliott Cowan, Albert Poon, Simon Rugera, Skating Panda Ltd
- Many companies who have given us advice
- Funding:
  - Grand Challenges Canada: Peter Singer, Ken Simiyu, Rebecca Lackman
  - Bill & Melinda Gates Foundation: Gene Walther, Christine Rousseau, Vincent Ahonkhai, Samuel Martins
- UNITAID: Brenda Waning