



# **Regulatory Convergence: to which Direction are we moving?**

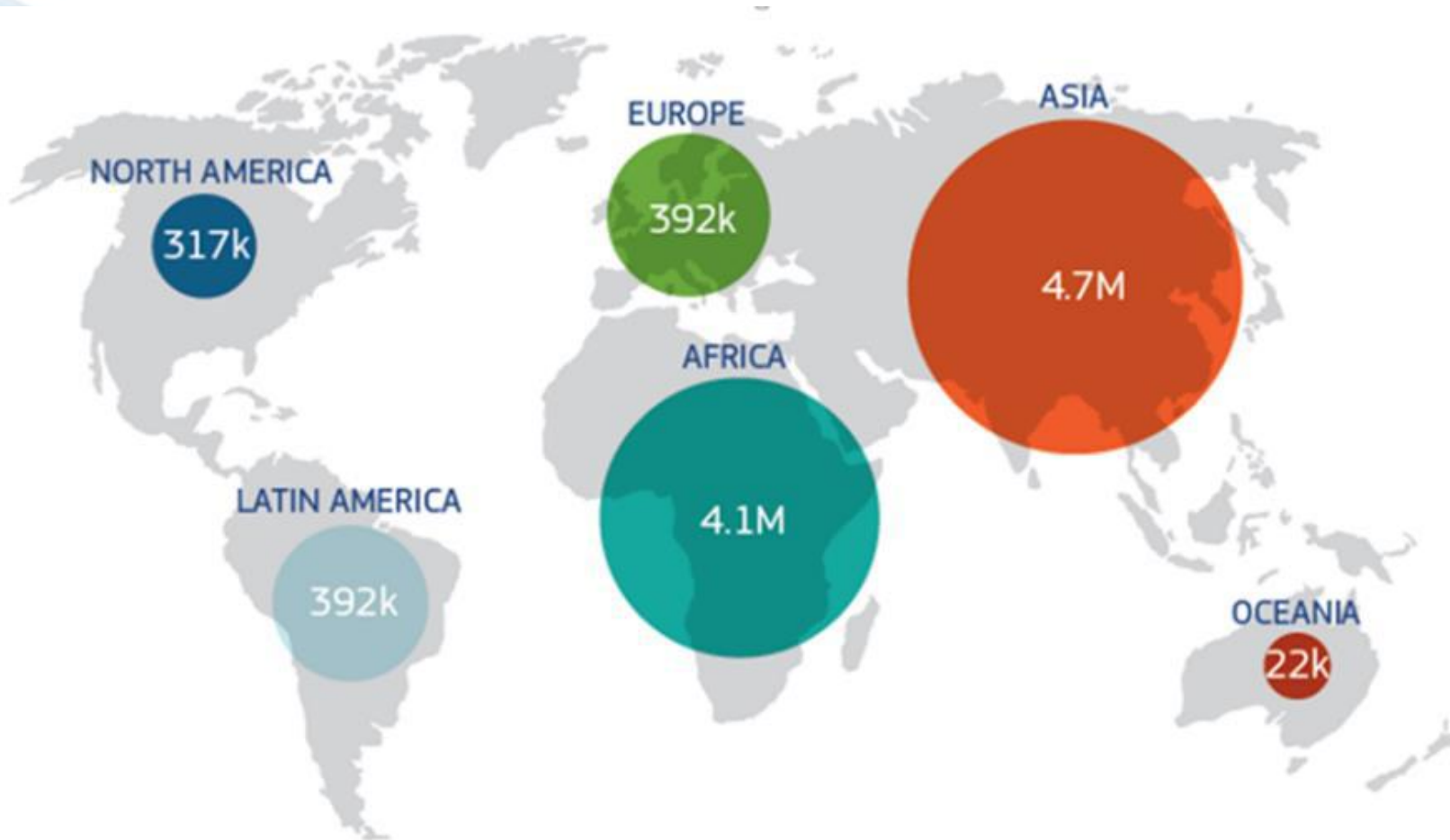
## **Updates on initiatives in Asia and Africa**

**Rosanna W Peeling**  
**Professor and Chair, Diagnostic Research**  
**Director, International Diagnostics Centre**  
**London School of Hygiene & Tropical**  
**Medicine**

# Regulatory Convergence

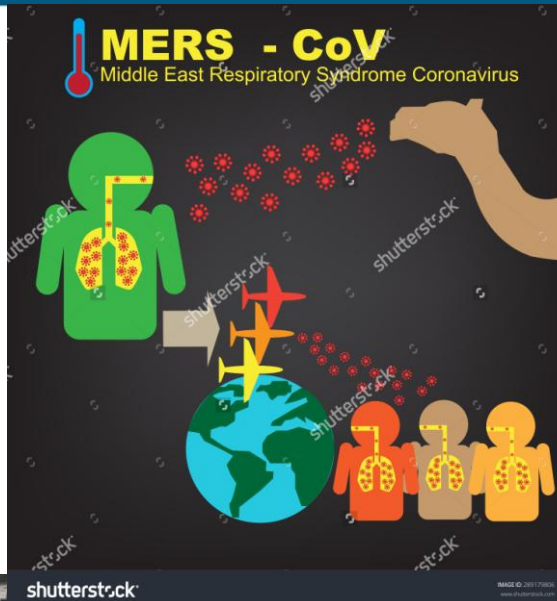
- **Rapid technological innovation driven by:**
  - Antimicrobial resistance (AMR)
  - Global health emergencies
  - Disease Elimination: 90-90-90 Targets for HIV, Dual and Triple elimination of HIV, Syphilis and Hepatitis B
  - Converging epidemics of infectious and non-communicable diseases
  - Connectivity to improve surveillance and health system efficiencies
- **Regulatory Convergence: to which direction are we moving?**
- **The way forward**

# # Lives lost/year attributable to Antimicrobial Resistance by 2050



(Source: European Commission)

# Global Health Emergencies: Need for Open Technology Platforms



## Dengue

**Dor atrás dos olhos**

Tontura      Manchas vermelhas

Dor nas articulações      Náuseas e vômitos

Fraqueza      Perda de peso

Febre alta      Dor de cabeça

Sangramento no nariz e na gengiva

## Chikungunya

**Dores intensas nas articulações de pés e mãos**      **Dor de cabeça**

Dor muscular      Manchas vermelhas

Febre alta

## ZikaV

**Dor nas costas**

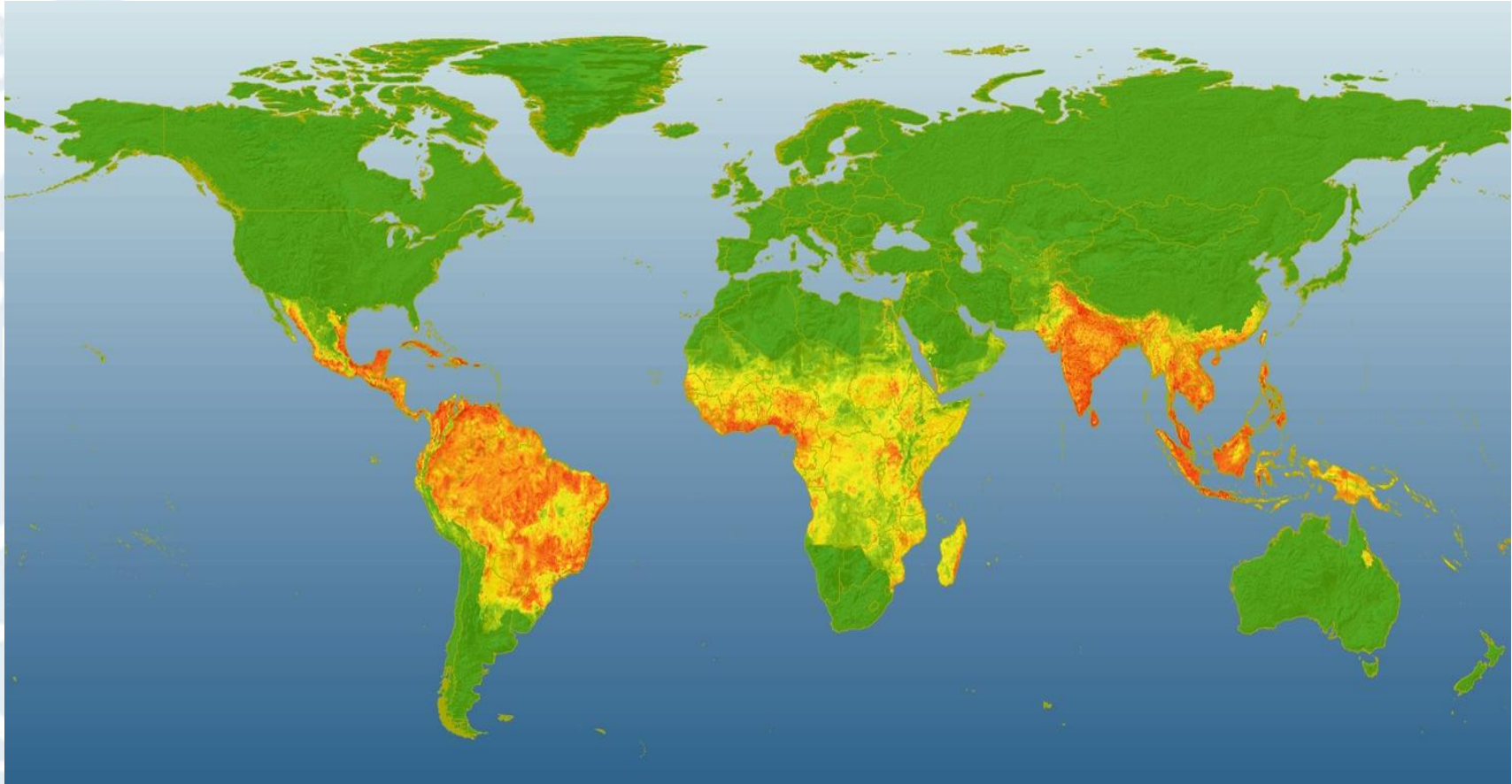
Olhos vermelhos

**Dor de cabeça**      **Lesões com pontos brancos e vermelhos na pele**

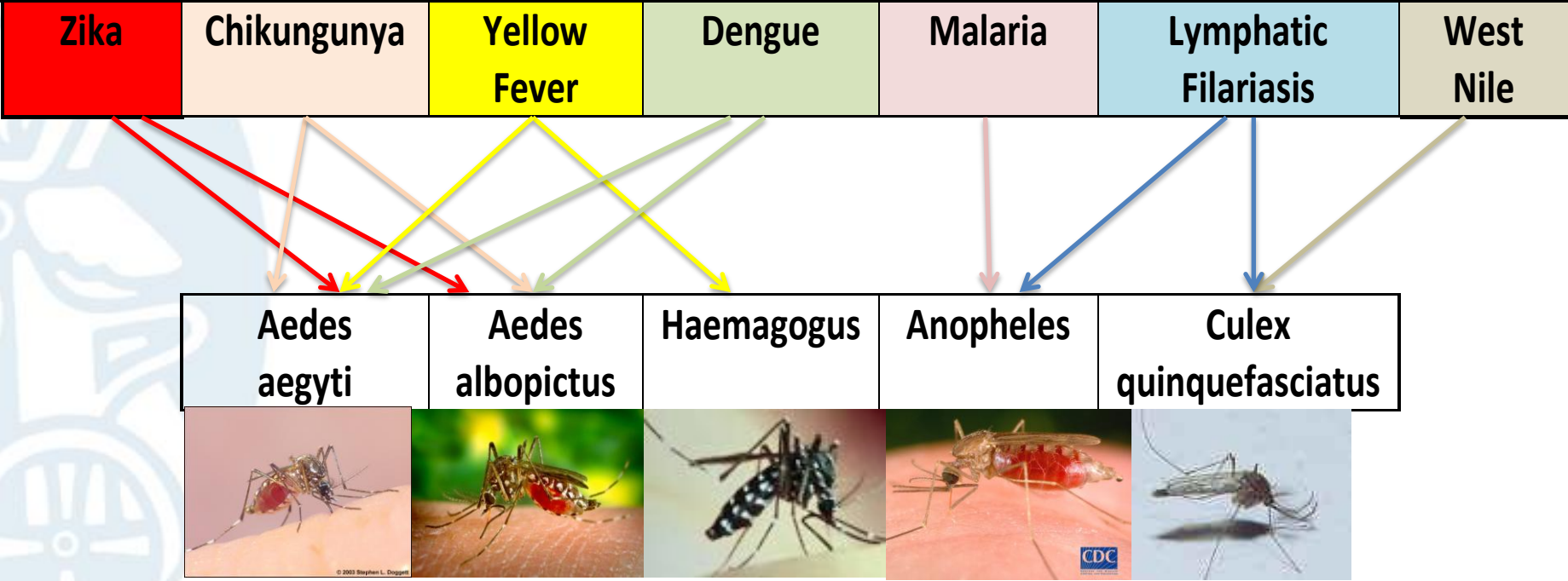
Dor muscular      Febre baixa      Dor nas articulações

Fonte: Ministério da Saúde

# Climate Change: The Expanding Dengue Belt



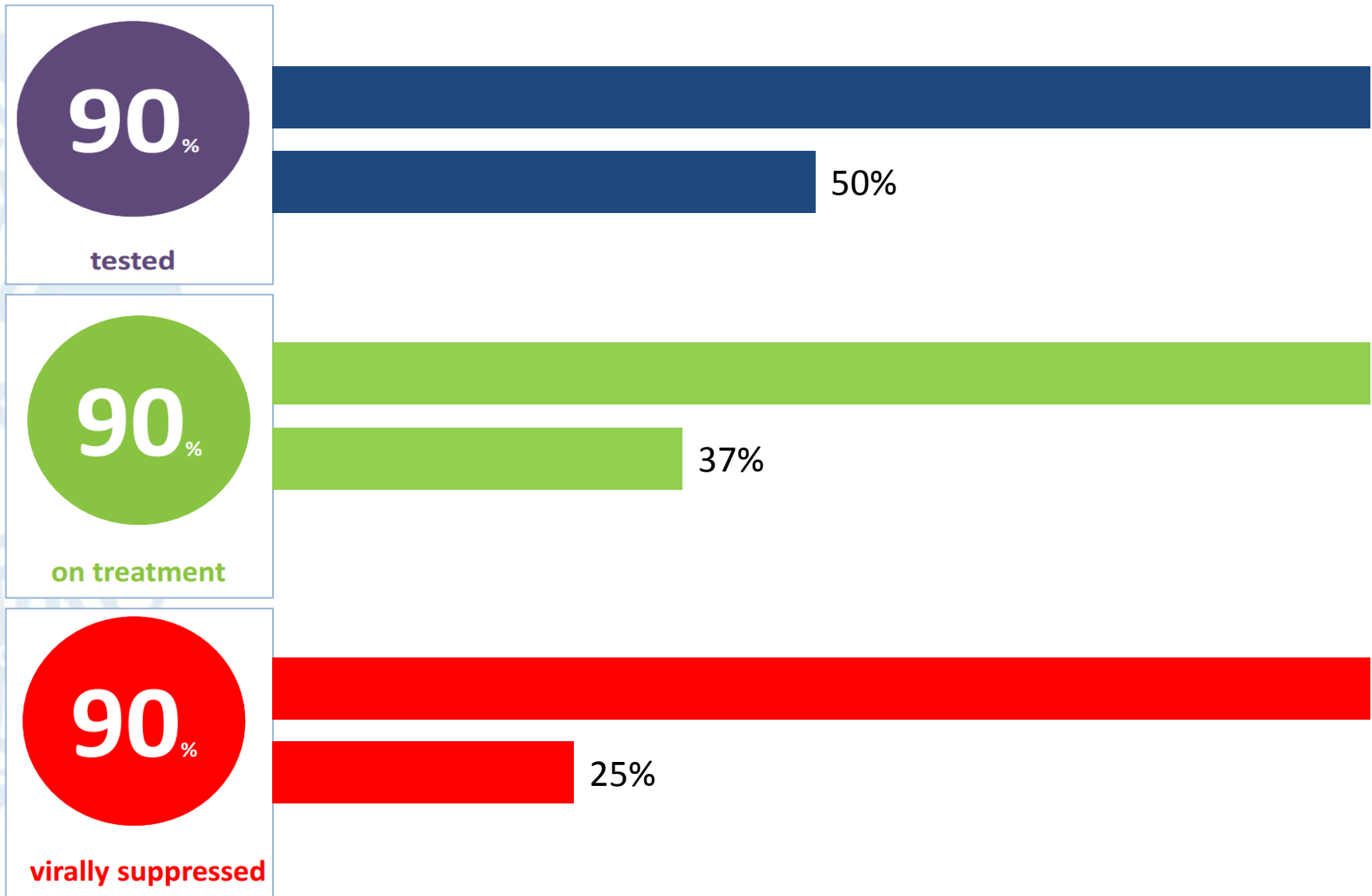
# Mosquito-borne Diseases: Humans vs Mosquitoes



# Preparing for the Inevitable

- **As part of the R&D Blueprint for Actions to Prevent Epidemics, WHO has called for ideas for platform technologies to improve research and development preparedness against a set of priority infectious disease threats:**
  - haemorrhagic fever: Crimean Congo, Ebola and Marburg, viruses, Lassa fever
  - MERS and SARS coronaviruses
  - Nipah virus, Rift Valley fever virus, Chikungunya and Zika viruses
  - Severe fever with thrombocytopenia
- **Although these platform technologies may be costly, compared to the cost of inaction, the investment is justified**
- **WHO has proactively engaged potential funders in the process in order to stimulate funding for the most promising ideas for open platform technologies to accelerate test development, validation, production and adoption**

# UNAIDS/WHO 2020 Targets for HIV





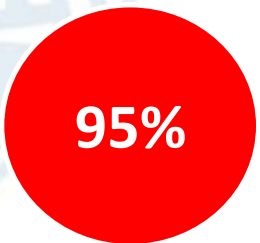
# Global Targets for eMTCT HIV/Syphilis



Access ANC



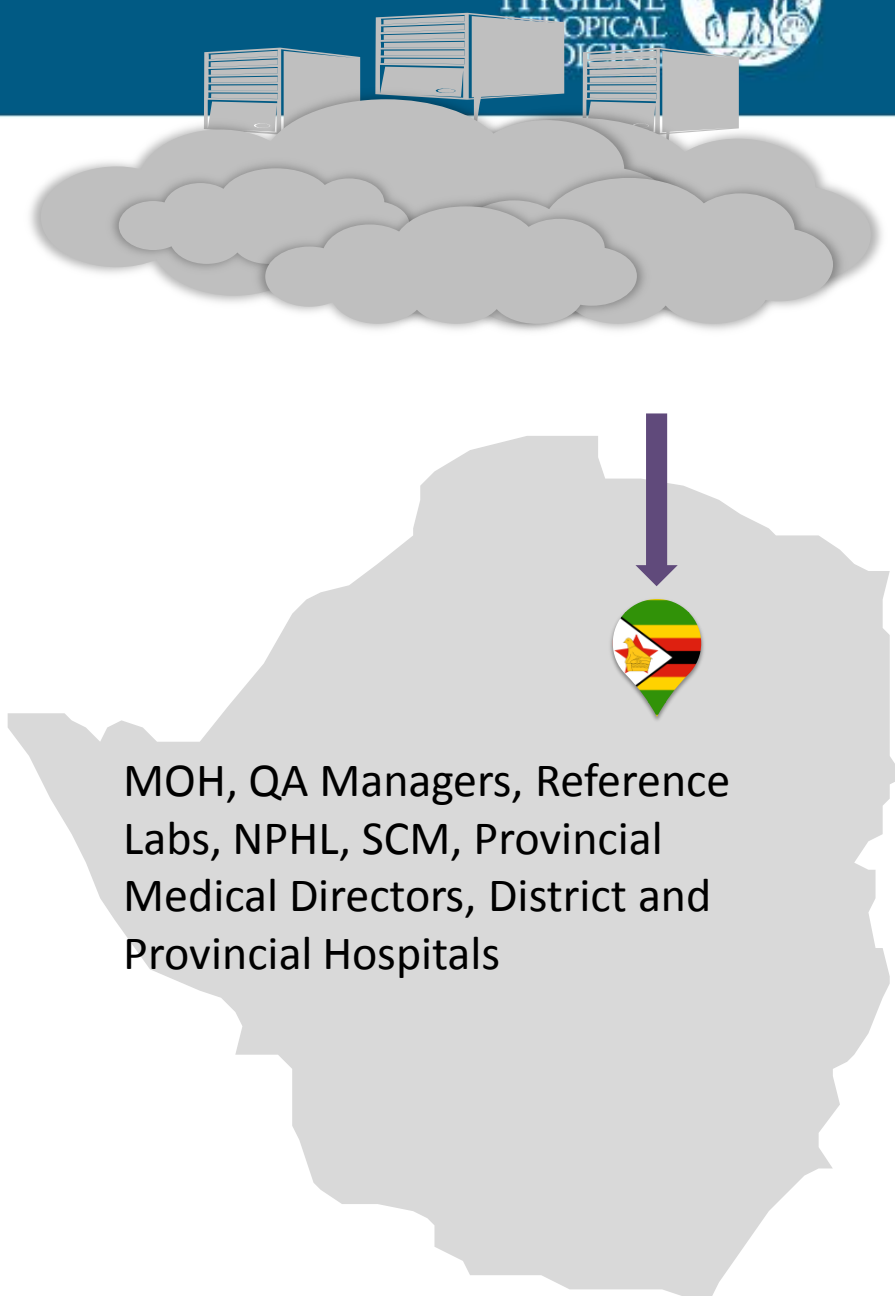
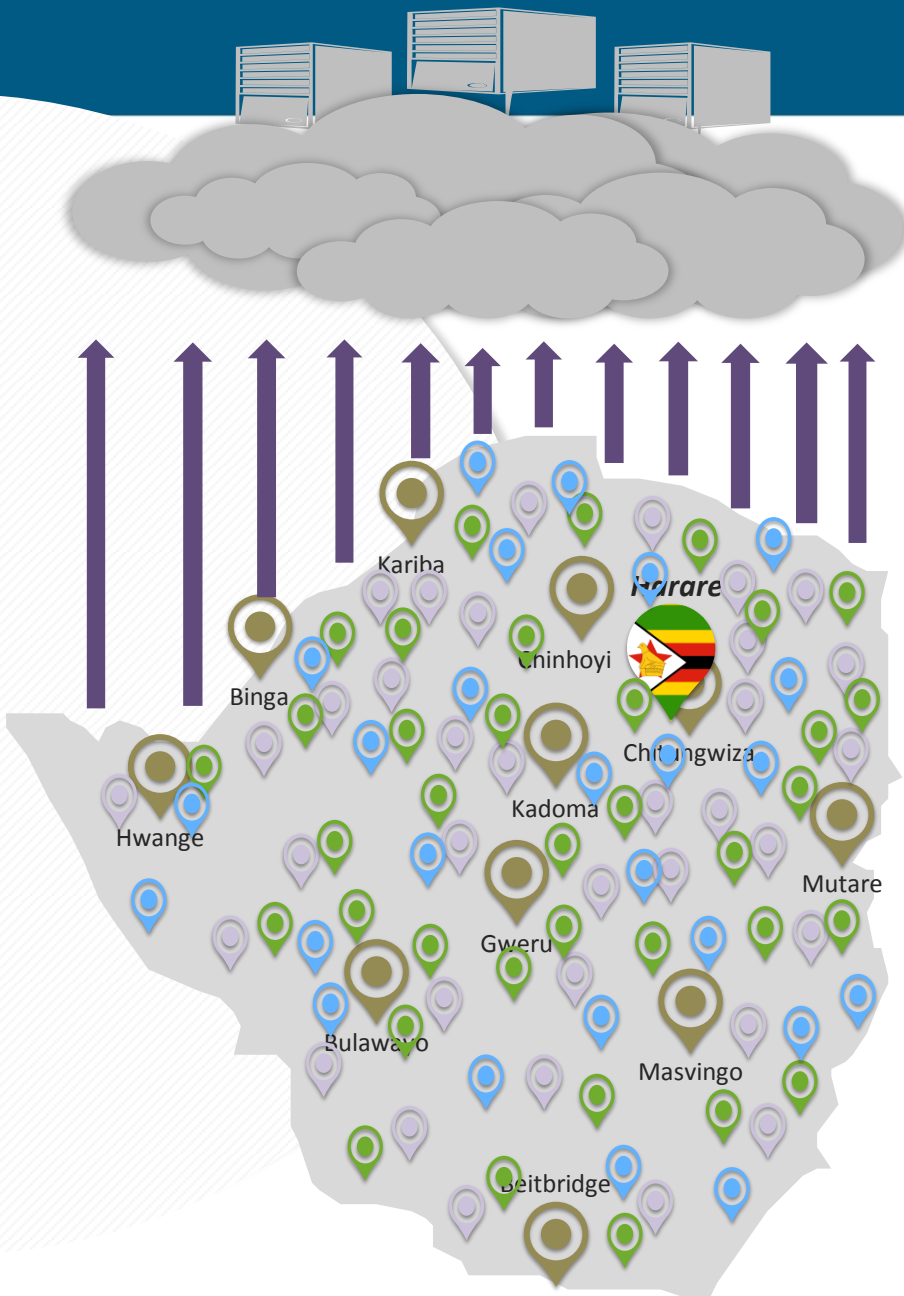
Tested for HIV & Syphilis



Treated



# The Need for Connectivity in Zimbabwe



# Converging Epidemics: TB and Diabetes



**Table 1** Summary data from reviews or reports on the prevalence of relevant infectious and non-communicable diseases in Sub-Saharan Africa

Source	Disease	Sub-group <sup>a</sup>	Men	Women	Total
Magadi, 2013 [3]	HIV	Poor: urban	-	-	9.2
		Poor: rural	-	-	5.3
		Non-poor: urban	-	-	7.3
		Non-poor: rural	-	-	6.2
WHO [6]	Tuberculosis	-	-	0.03	
WHO [10]	Obesity	5.3	11.1	-	
Ataklte [8]	Hypertension	-	-	30	
Hilawe [13]	Diabetes	5.5	5.9	5.7	

<sup>a</sup>Study-specific socio-demographic characteristics

These 2 conditions influencing one another by multiple pathways [Dooley 2009].

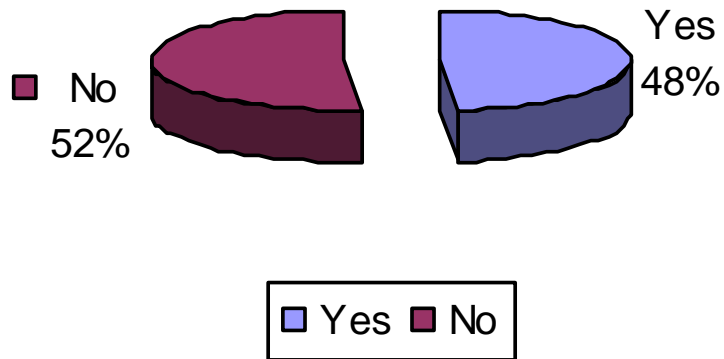
- Diabetes impairs the immune responses needed to control bacterial infections, thereby increasing susceptibility to TB
- A systematic review of cohort studies found that individuals with diabetes have a 3-fold greater risk of developing active TB infection, compared to without [Jeon et al 2008]
- Type 2 diabetes is expected to rise in Africa by 110 % from 19.8 million in 2013 to 41.5 million in 2035

# Regulatory Convergence

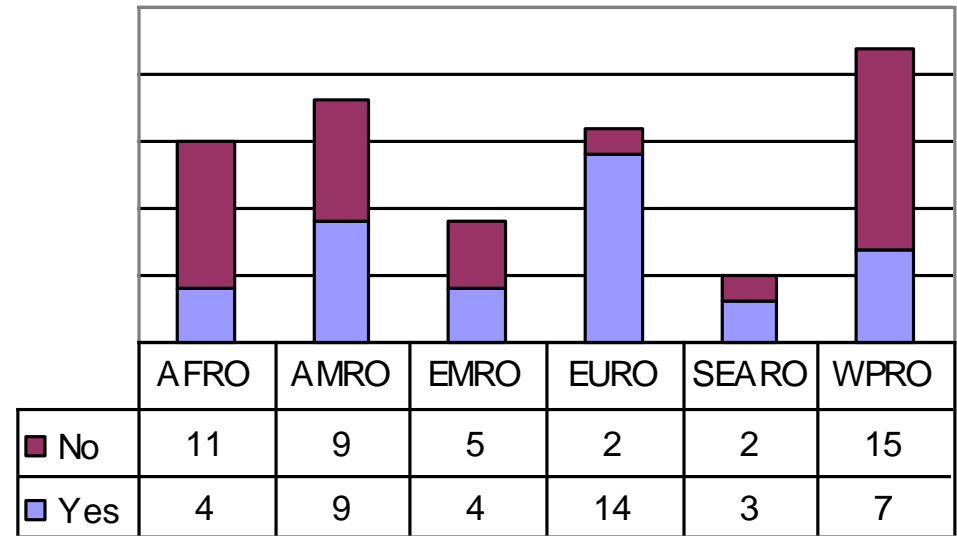
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# Regulatory Oversight of *in-vitro* Diagnostics

## In Vitro Diagnostic Devices Regulated



## In Vitro Diagnostic Devices Regulation By Region



WHO/TDR survey 2002

# Regulation of In-vitro Diagnostics in the Developing World

1. The primary goal of regulation is to protect public health and safety
2. A regulatory system should ensure that valuable new technologies are made available to the clinical community and to patients and consumers expeditiously while preventing unsafe and ineffective devices from reaching the market
3. Regulatory decisions must be based on strong and clear science

Extracted from:  
A model regulatory program for medical devices: an international guide. WHO & FDA, 2001

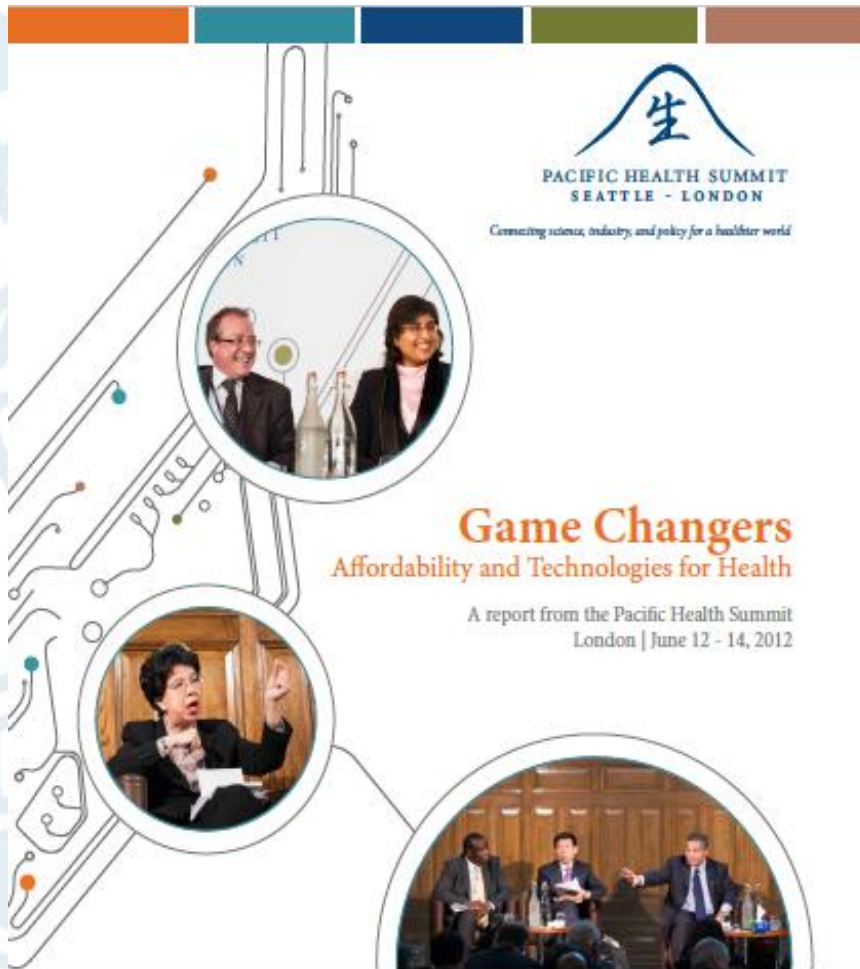
1. Regulatory landscape for IVDs highly variable
2. Many countries have a legal framework and policy for medical devices but lack capacity for implementation
3. The process of approval is often costly, lengthy and not transparent
4. Many IVDs are sold and used without evidence of effectiveness, leading to waste of precious resources and in some cases, wrong diagnosis

Ref: McNerney & Peeling. Clin Infect Dis. 2015 Oct 15;61 Suppl 3:S135-40

# Pacific Health Summit 2012

## Game Changers

LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



Call for regulatory systems  
that are faster, better,  
safer and cheaper

NBR THE NATIONAL BUREAU  
OF HEALTH RESEARCH

FRED HUTCHINSON  
CANCER RESEARCH CENTER  
A LIFE OF SCIENCE

BILL & MELINDA  
GATES foundation

wellcome trust



PACIFIC HEALTH SUMMIT  
SEATTLE - LONDON

# “Faster, Better, Safer, Cheaper? Regulatory Opportunities”

LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



**Rosanna Peeling**, Professor,  
London School of Hygiene &  
Tropical Medicine

**Trevor Mundel**, President of  
the Global Health at the Bill &  
Melinda Gates Foundation

**Michael Watson**, VP of Global  
Immunization Policy at Sanofi  
Pasteur

**Rhona Applebaum**, VP and  
Chief Scientific & Regulatory  
Officer, Coca-Cola Company

The purpose of this panel is to examine the relationship between regulation and innovation, and explore ways in which regulation can be utilized to stimulate innovation, avoid regulatory bottlenecks, inefficiencies, and inconsistency to reduce costs and to accelerate access.

**Regulators should add value and be a part of the quality system, not an audit system, which comes after the fact and tries to establish guilt.**

Trevor Mundel, President, Global Health,  
Bill & Melinda Gates Foundation



# East African Community (EAC)

- A regional intergovernmental organisation:



**Kenya**



**Uganda**



**Tanzania**



**Rwanda**



**Burundi**

- EAC was established in 1999, with a treaty ratified by the original 3 Partner States – Kenya, Uganda and Tanzania. Rwanda and Burundi became full Members in 2007. Its headquarters: Arusha, Tanzania
- **Vision:** a prosperous, competitive, secure, stable and politically united East Africa
- Launched **the EAC Medicines Registration Harmonization Project** on 30 March 2012 in Arusha, Tanzania with support from the African Union's New Partnerships for African Development (AU-NEPAD), WHO, World Bank, BMGF, Clinton Health Access Initiative, DFID, GIZ and others.
- **EAC Secretariat approached LSHTM in April 2012 to initiate discussions on harmonization of diagnostics, which led to a meeting in September 2012 with all 5 members of EAC and Ethiopia, Nigeria and South Africa**



ALAD DiV

# Advanced Course on Diagnostics, Annecy, France, September 2012



Rosanna Peeling , Carlos Gouvea , Adele Benzaken, Graciela Russomando  
Alain Mérieux, Patricia Velez Moller and Segundo Leon

# Pan-African Harmonization Working Party



Founded in Dec 2012 to steer regulatory harmonization activities in the region in partnership with the Asian Harmonization Working Party (AHWP), ALADDIV, the African Union, and WHO AFRO

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 Executive:

Chair: EAC (Tanzania)

Vice-Chair: Nigeria

Secretariat: South Africa

3 African Regulatory Fora for Medical Diagnostics were held on July 2013, Feb and Nov 2014 funded by the Bill & Melinda Gates Foundation and Grand Challenges Canada

# Pan African Harmonization Working Party



- **Vision**: valuable, quality assured, safe medical devices and diagnostics are made available where needed
- **Mission**: to protect public health
- **Goal**: to study and recommend ways to harmonize medical devices and diagnostics regulation in Africa

## Priorities for Harmonization:

- Common Registration File (WHO PQ dossier)
- Risk Classification (Global Harmonization Task Force)
- Quality Systems Audit (IMDRF)
- Clinical Evidence (Joint review of data)
- Post Market Surveillance

# Survey of *in-vitro* Diagnostics (IVDs) Regulation in Africa



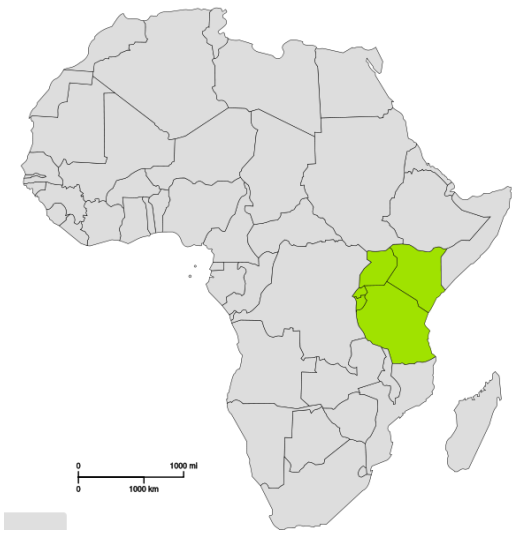
Regulations	Burundi	Kenya	Rwanda	Tanzania	Tanzania/ Zanzibar	Uganda	Ethiopia	Nigeria	South Africa
Legal framework	✓	✓	✓	✓	✓	–	✓	✓	✓
IVD regulated?	–	✓	–	✓	✓	–	✓	✓	✓
Premarket controls									
Adoption of GHTF classification	–	–	–	✓	✓	–	✓	In process	✓
Registration	–	+	–	✓	–	–	✓	✓	✓
Clinical performance	+	✓	–	✓	–	✓	✓	–	✓
Evaluation capacity				Limited		HIV only	Limited		
Manufacturing audit	–	–	–	–	–	–	–	–	–
Marketing controls									
Advertising control	✓	+	–	✓	–	✓	✓	✓	✓
Marketing controls	–	+	HIV, TB	✓	–	✓	✓	✓	✓
Postmarketing controls									
Surveillance	–	+	–	✓	–	–	–	–	✓
Accredited laboratories	–	✓	–	✓	–	✓	✓	–	✓
Device reporting	–	+	–	–	–	–	–	–	✓
Corrections/recall	–	+	–	–	–	–	–	–	✓

Abbreviations: GHTF, Global Harmonization Task Force; HIV, human immunodeficiency virus; IVD, in vitro diagnostics; TB, tuberculosis.

# IVD Regulation in the East African Community



Country	Documents reviewed	Organisations interviewed (Number of persons)
Burundi	1	<ul style="list-style-type: none"> <li>i. Ministry of Health</li> <li>ii. Directorate of Pharmacies, Medicines and Laboratories</li> </ul>
Kenya	17	<ul style="list-style-type: none"> <li>i. Pharmacy and Poisons Board (3)</li> <li>ii. National Quality Control and Medical Devices Laboratory</li> <li>iii. Kenya Medical Laboratory Technicians and Technologists Board (2)</li> </ul>
Rwanda	4	
Tanzania (Mainland)	11	<ul style="list-style-type: none"> <li>i. Tanzania Food and Drugs Authority (2)</li> <li>ii. Private Health Laboratories Board</li> </ul>
Tanzania (Zanzibar)	6	<ul style="list-style-type: none"> <li>i. Zanzibar Food and Drugs Board (2)</li> <li>ii. Central Medical Stores, Ministry of Health and Social Welfare</li> <li>iii. Chief Pharmacist, Ministry of Health and Social Welfare</li> </ul>
Uganda	8	<ul style="list-style-type: none"> <li>i. National Drug Authority (3)</li> <li>ii. Pharmacy Division, Ministry of Health</li> <li>iii. Uganda National Bureau of Standards (2)</li> <li>iv. Allied Health Professionals Council</li> <li>v. Medilab (Laboratory supplies company)</li> <li>vi. Central Public Health Laboratories</li> </ul>
<b>Total</b>	<b>47</b>	<b>16 (24)</b>



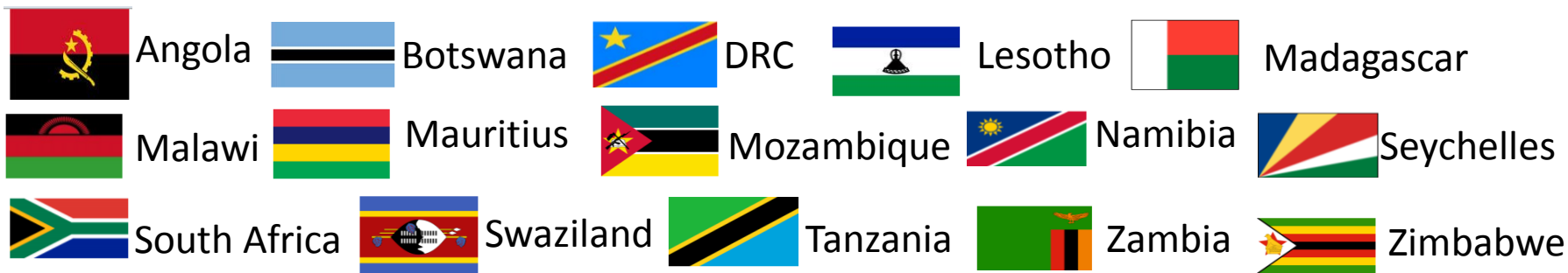
Rugera et al. BMC Health Services Research 2014;14:524



# Southern Africa Development Community (SADC)



- Established in 1980 as a development coordinating conference (SADCC)
- Transformed in 1992 into a development community
- An inter-governmental organisation to promote sustainable and equitable economic growth and socio-economic development through efficient productive systems, deeper co-operation and integration, good governance and durable peace and security among 15 Southern African countries





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.

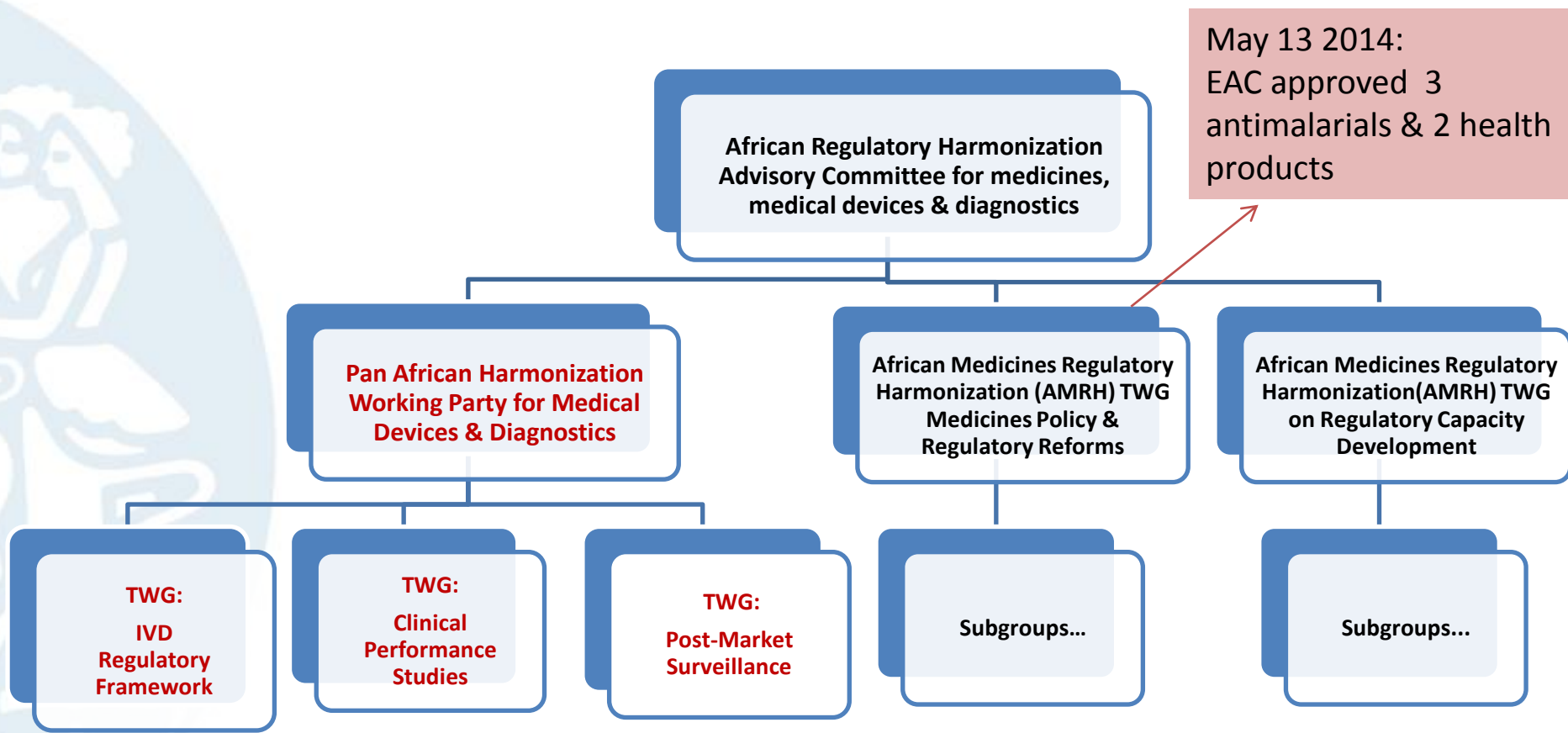
The 4 countries share several commonalities and face similar challenges regarding medicine regulations which created an opportunity for a mutually beneficial collaboration.

The benefits include:

- reduction of regulatory workload
- accelerated registrations of required products
- mutual trust and confidence in regulatory collaboration
- improved information sharing and networking

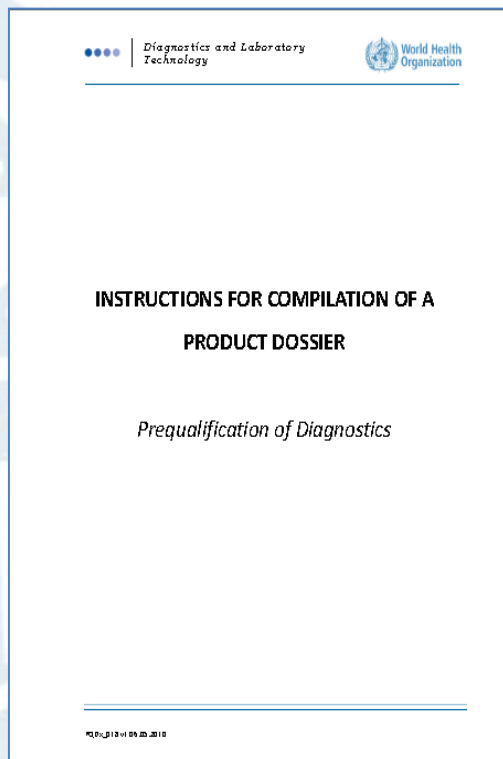


# 2013: PAHWP is hosted within the African Union-NEPAD Planning & Coordinating Agency



May 13 2014:  
EAC approved 3 antimalarials & 2 health products

# Common Registration File and Post-marketing Surveillance



## 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



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

# Training on Review of Clinical Performance data from HIV POC Test Evaluations in 2014

Faculty:  
LSHTM  
WHO PQ  
Regulatory consultant



**PAHWP - EAC - LSHTM TRAINING WORKSHOP ON ASSESSMENT OF CLINICAL PERFORMANCE OF IVDS  
3<sup>rd</sup> - 4<sup>th</sup> JULY 2014 AT KIBO PALACE HOTEL  
ARUSHA - TANZANIA**

Creation of Virtual Campus

- e-learning materials
- mentoring online
- face to face workshops



**ADVANCED TRAINING WORKSHOP 20-23<sup>rd</sup> OCTOBER 2014 DAR ES SALAAM**

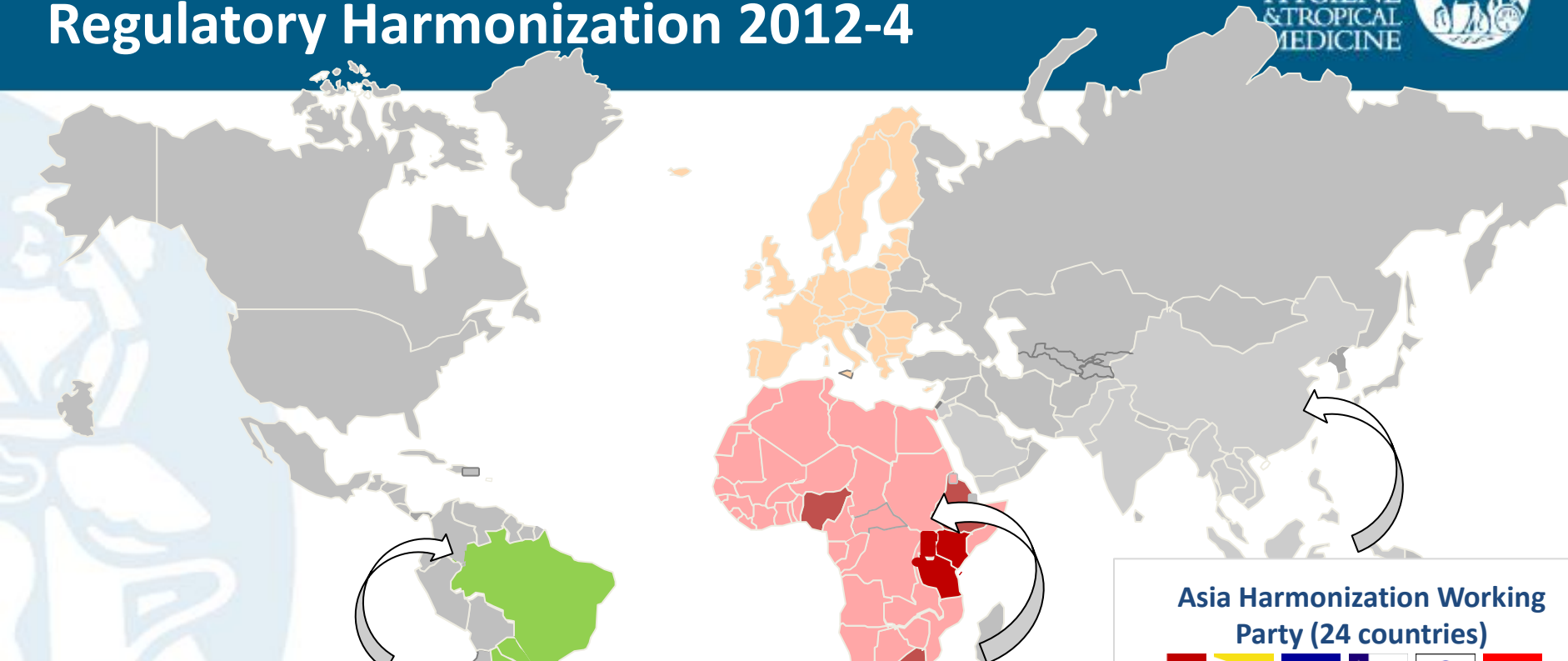


Grand Challenges Canada™  
Grands Défis Canada<sup>MC</sup>

**BOLD IDEAS FOR HUMANITY.™**



# Progress towards IVD Regulatory Harmonization 2012-4



**Latin America Diagnostic Alliance (ALADDIV) (12 countries)**



**Pan-African Harmonization Working Party (15 countries)**



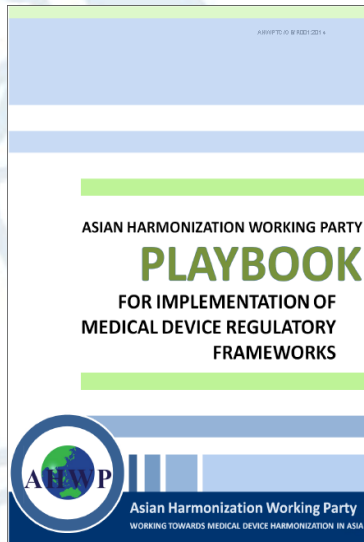
**Asia Harmonization Working Party (24 countries)**



# Regulatory Convergence

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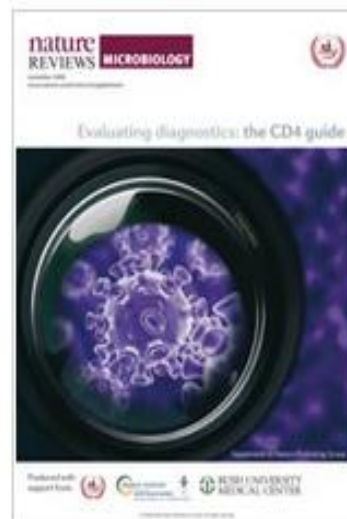
## Building Regulatory Capacity using Harmonized Approaches



- Courses on review of performance studies
- Joint review of data
- Leverage MDSAP data
- Sharing post-market surveillance data

## Advancing Regulatory Science

- Regulation to keep pace with technological innovation
- Institutes of Regulatory Science



## Re-convening the Regulatory Forum

- Neutral Platform for:
  - Convergence
  - standardization
- Open dialogue on regulatory science and technological innovation
- Sharing of country and industry experiences

# PAHWP Updates 2015-6



- Membership: 15 Countries  
EAC: Kenya, Tanzania, Uganda, Rwanda, Burundi  
Ethiopia, Nigeria, South Africa  
Ghana, Malawi, Mozambique, Senegal, Sierra Leone, Zambia, Zimbabwe
- Tanzania became a member of the AHWP in Nov 2014
- Ghana, Kenya, and Zimbabwe are members of the IVD Working Group of AHWP
- PAHWP as a liaison member of ISO working group on POC devices under discussion
- A Joint Regulatory Forum at the African Society for Laboratory Medicine Conference on Dec 4-8 in Cape Town, South Africa is being planned

# Thank you

- **LSHTM:** Ruth McNerney, Debi Boeras, Maurine Murtagh, Ben Cheng
- **AU:** Paul Tanui
- **EAC:** Stanley Sonoiya, Jane Masingia, Louisa Kosimbei
- **WHO:** Jean-Bosco Ndiokubwayo, Willie Urassa, Robyn Meurant
- **ASLM:** Trevor Peter, Tsehaynesh Messele
- **GIZ:** Wesley Ronoh, Thomas Walter
- **PAHWP:** Issac Kadowa, Ilonze Chinyere, Sagie Pillay, Sarvashni Moodliar, Patience Dabula, Agnes Kijo
- **AHWP:** Liling Liu, Albert Poon, Jeffrey Chern, Jack Wong, Benny Ons
- **ALADDIV:** Carlos Gouvea, Adele Benzaken, Freddy Tinajeros 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, Bill & Melinda Gates Foundation