Update
WHO Activities in Medical Device Regulation

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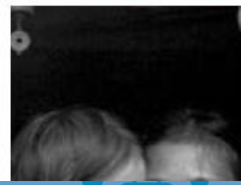
World Health Organization

2016


Universal health coverage
The International Health Regulations (2005)
Increasing access to medical products
Social, economic and environmental determinants
Noncommunicable diseases
including disabilities, mental health, violence and injuries
Health-related Millennium Development Goals
WHO leadership priorities



Progress towards the Sustainable Development Goals

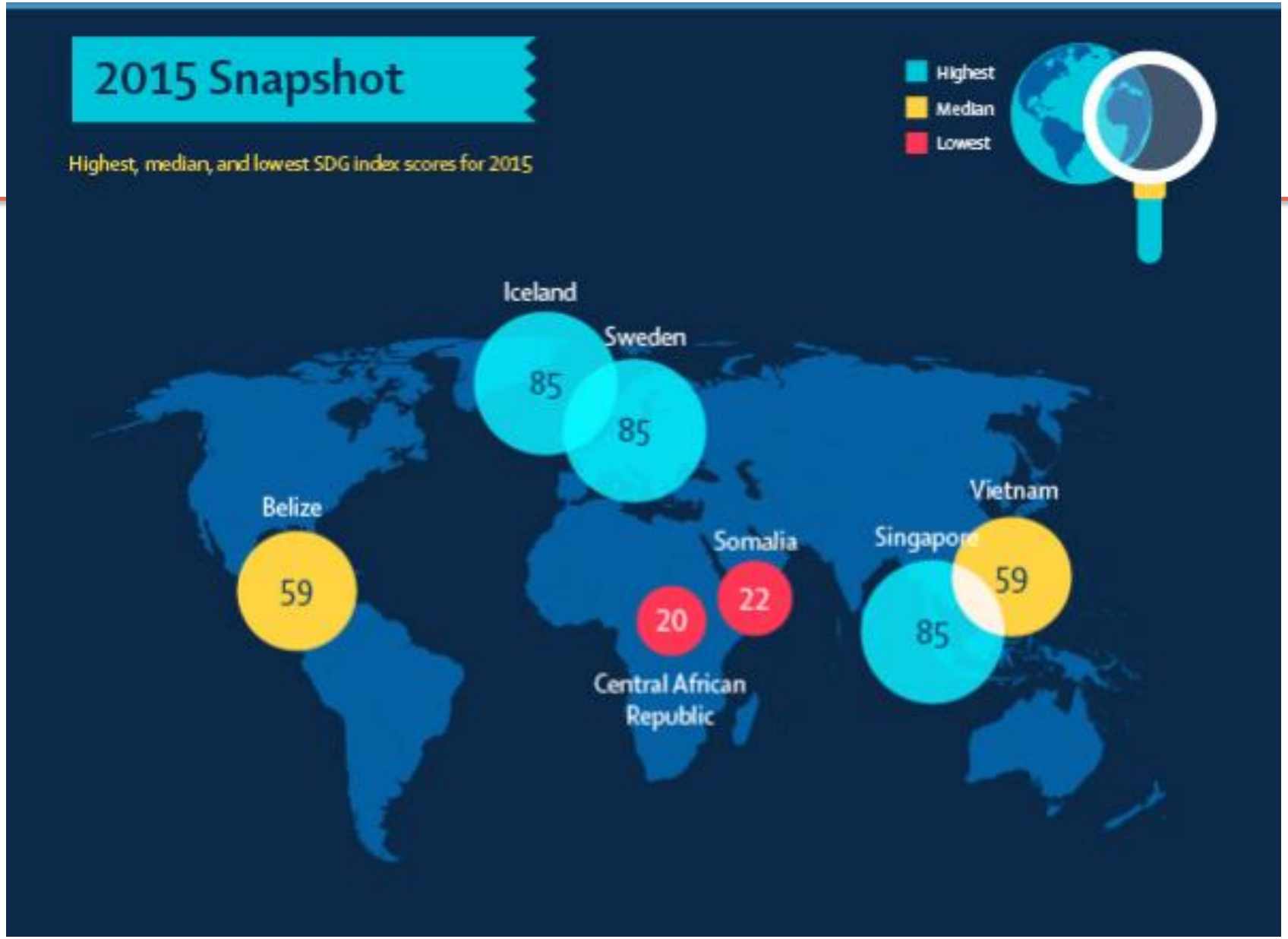
What are the Sustainable Development Goals?

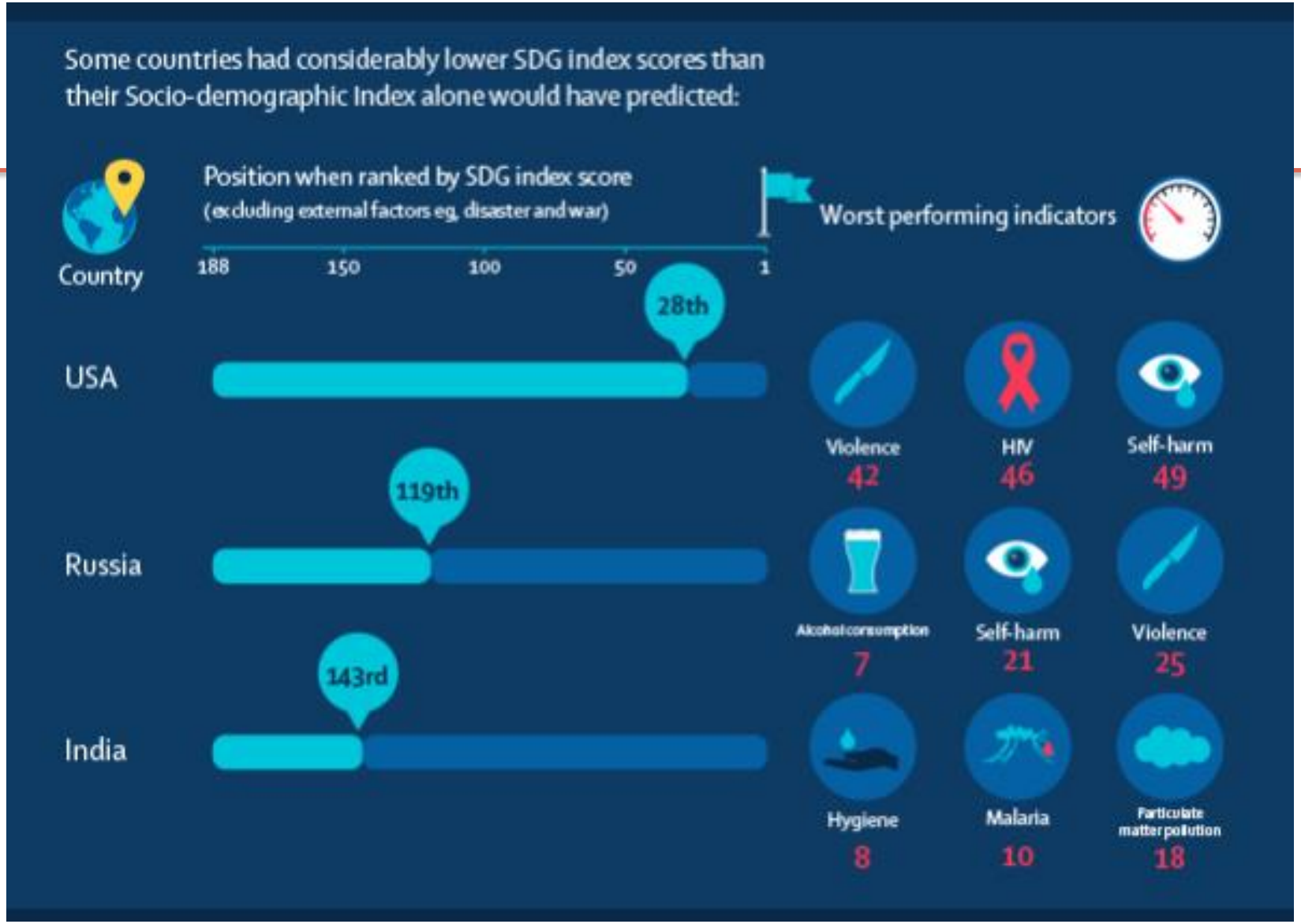
In September, 2015, the United Nations General Assembly established the Sustainable Development Goals (SDGs) to replace the Millennium Development Goals, which expired in 2015. The SDGs specify:

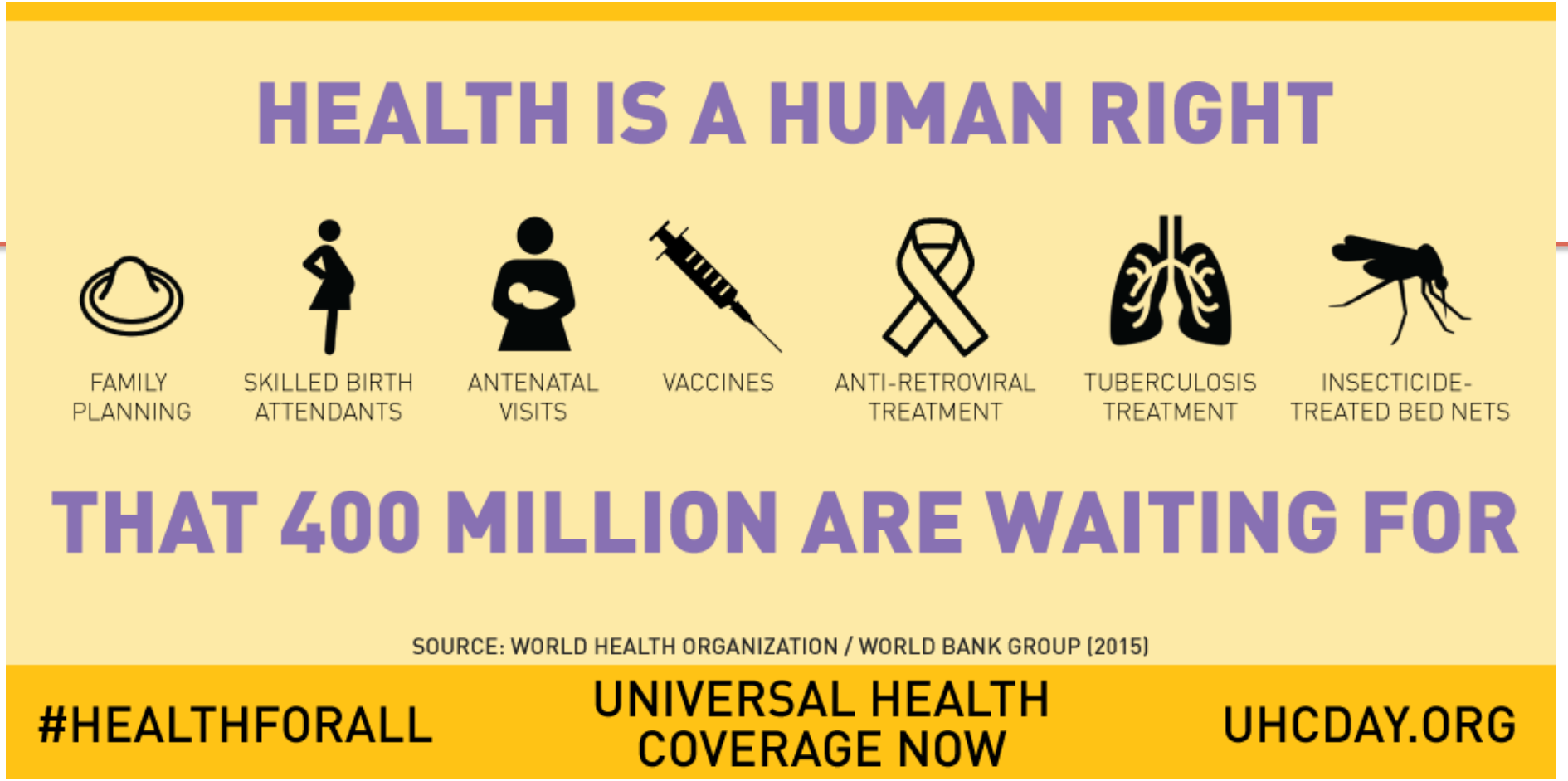
17 universal goals + **169** targets + **230** indicators → 2030 leading up to 2030

To allow for easier comparison, an indexed score has been created for each health-related indicator, with the worst observed value in the period 1990–2015 rated as zero, and the best as 100[1].

The Lancet 2016


2015 Snapshot
Highest, median, and lowest SDG index scores for 2015
Highest
Median
Lowest
Iceland
85
Sweden
85
Belize
59
Somalia
22
20
Central African Republic
Vietnam
59
Singapore
85

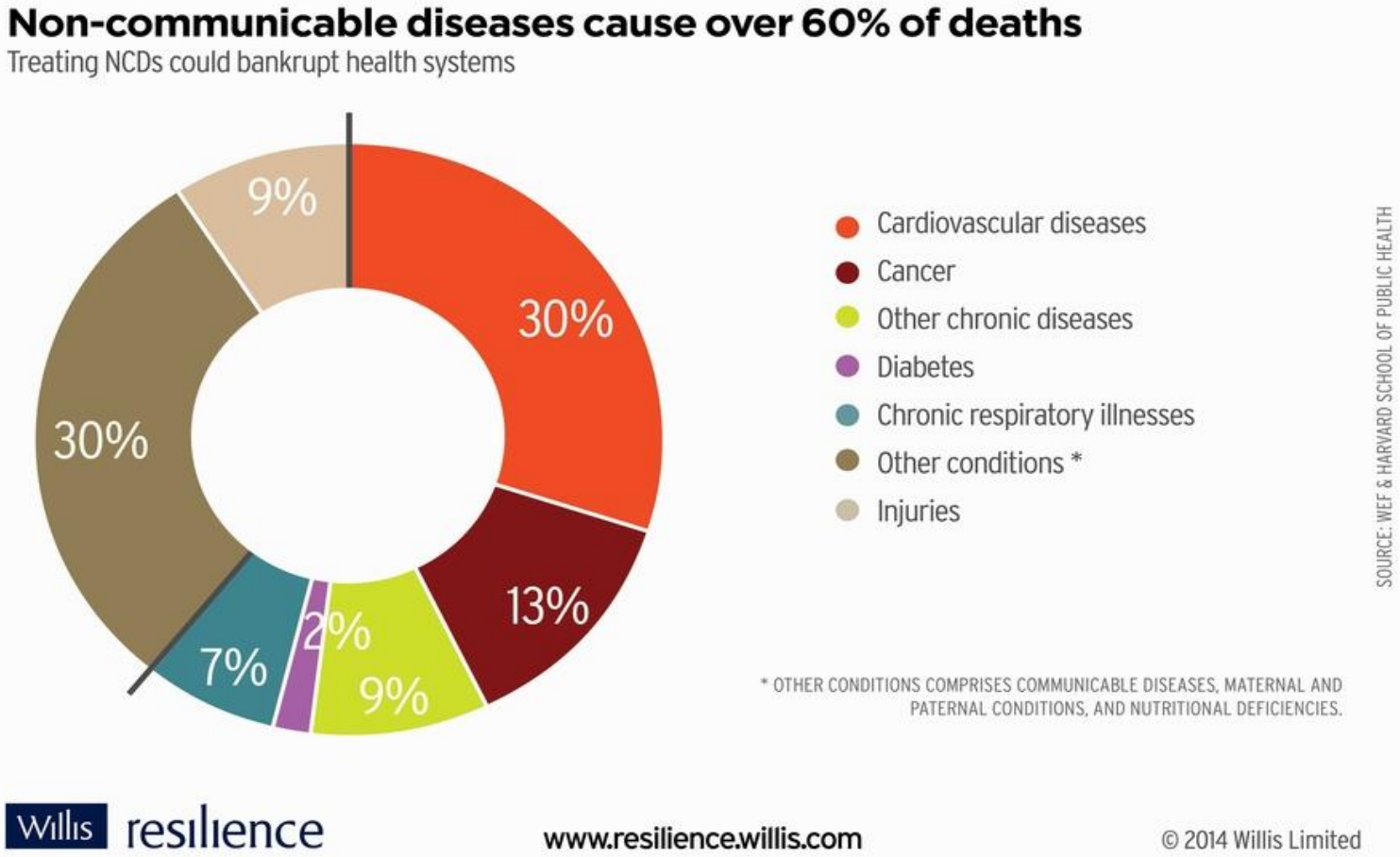

Some countries had considerably lower SDG index scores than their Socio-demographic Index alone would have predicted:
Country
Position when ranked by SDG index score
(excluding external factors eg, disaster and war)
188
150
100
50
1
Worst performing indicators
USA
28th
Violence
42
HIV
46
Self-harm
49
Russia
119th
Alcohol consumption
7
Self-harm
21
Violence
25
India
143rd
Hygiene
8
Malaria
10
Particulate matter pollution
18



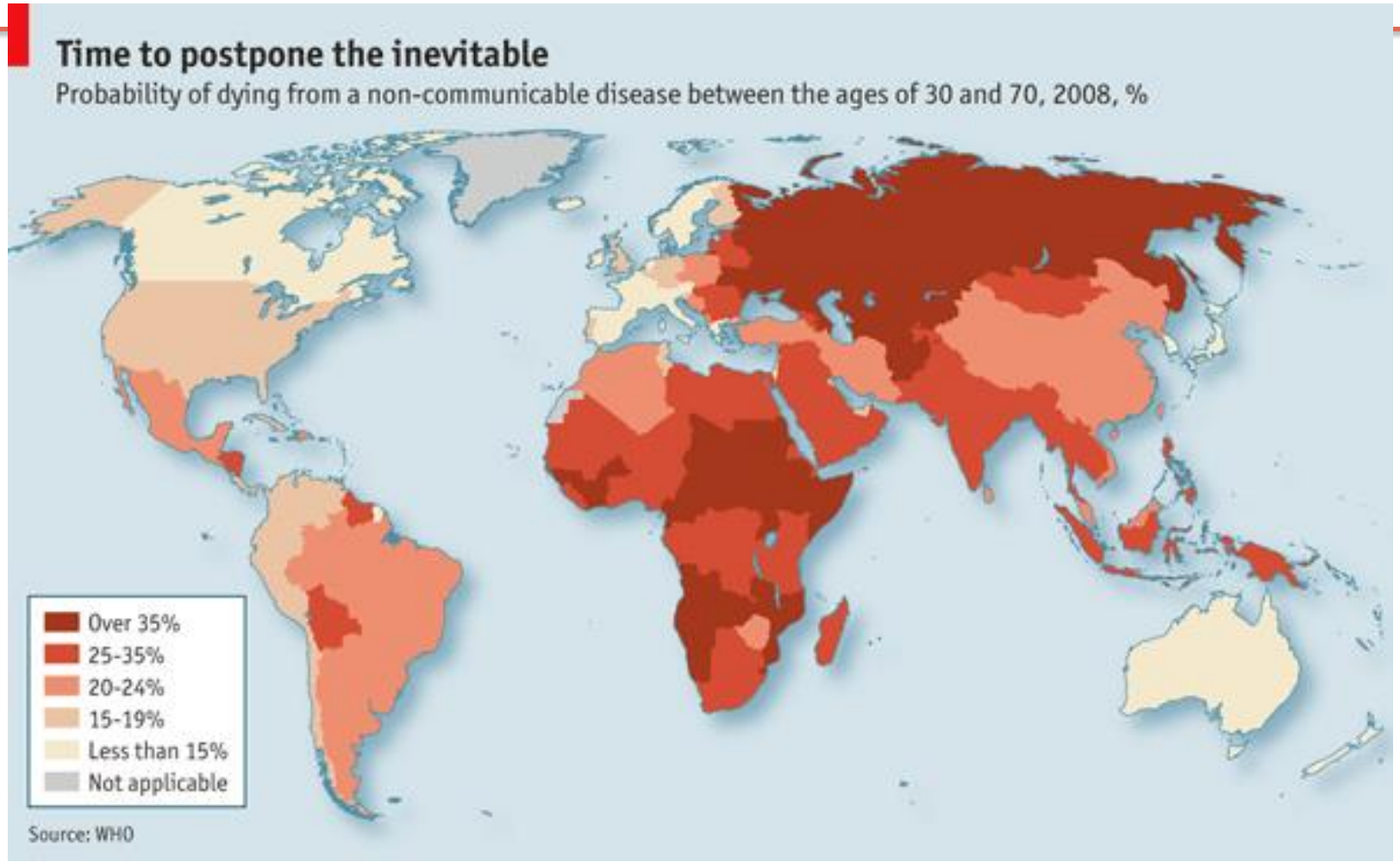
Goal:

All people receive the health services they need without suffering financial hardship

Non-communicable diseases



Non-communicable diseases



Increasing access to medical products

❖ 22,000 Types of medical devices

❖ 5,000,000 different products commercially available*

- Diagnostic imaging
- Laboratory and pathology equipment
- Implantable medical devices
- All medical equipment for patient care
- Single use devices (IV)
- Personal protective equipment
- Prosthesis and orthesis
- Quality assurance
- Radiation protection
- Solutions and reagents
- Surgical instruments
- Sterilization equipment….

*WHO GLOBAL MODEL REGULATORY FRAMEWORK

WHO Resolution …promoting equitable access to quality, safe, efficacious and affordable medical products

SIXTY-SEVENTH WORLD HEALTH ASSEMBLY **WHA67.20**

Agenda item 15.6 **24 May 2014**

Regulatory system strengthening for medical products

The Sixty-seventh World Health Assembly,

Having considered the report on regulatory system strengthening; [1]

Welcoming the efforts of the Director-General, and recognizing the pivotal role that WHO plays in supporting countries in strengthening their regulatory systems of medical products for human use, [2] and in promoting equitable access to quality, safe, efficacious, and affordable medical products;

2017 A year of change

- Not only the long awaited EU Regulations but also, some major changes at WHO

New DG

New ADG, HIS

Changes in HIS

- Director,

Essential Medicines and Health Products (EMP)

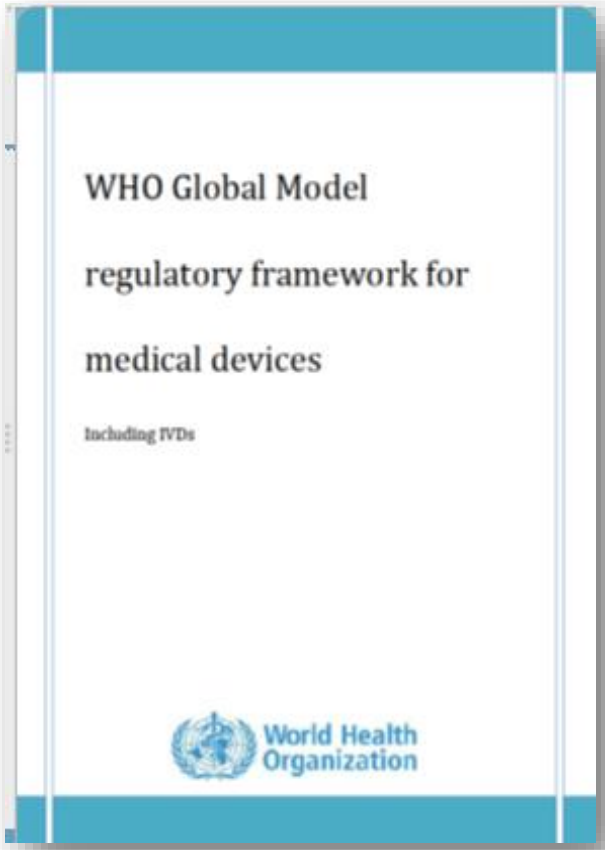
  - Dr Suzanne Hill

- Head,

Regulation of Medicines and Other Health Technologies (RHT)

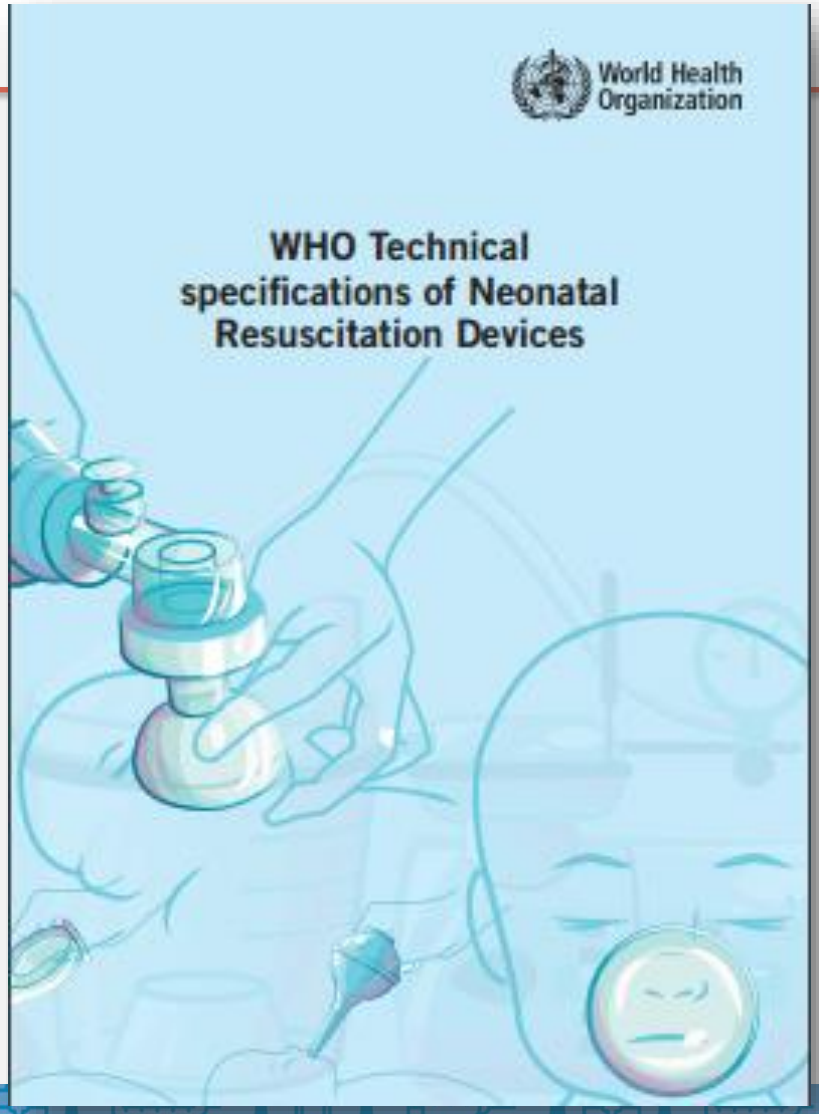
  - Dr Emer Cooke

Policy, Access and Use



- Based on GHTF/IMDRF principles and concepts developed in the AHWP Playbook
- Two step approach
  - Basic level controls and enforcement
    - Legal framework
    - Market oversight
    - Reporting system
  - Expanded level controls and enforcement
    - regulatory controls depending on the priorities of the country

Policy, Access and Use



Health technology management of medical devices

WHO technical specifications of neonatal resuscitation devices
2016

WHO technical specifications for oxygen concentrators
2015

2015 Rapid Guidance on the Decommissioning of Ebola Care Facilities
2015

Manual for Procurement of Diagnostics and Related Laboratory Items and Equipment
2013

Medical equipment maintenance programme overview
2011

Needs Assessment for Medical Devices
2011

Procurement Process Resource Guide
2011

Medical Device Donations: Consideration for Solicitation and Provision
2011

Introduction to Medical Equipment Inventory Management
2011

Computerized Maintenance Management System
2011

Maintenance Manual for Laboratory Equipmentstem
2008

Innovation

- Priority Assistive Devices List

Access	LMIC	Need
1 in 10	**3%**	**2 billion**
has access to assistive technology	of the population in need has access to hearing aids	population will need assistive technology by 2050

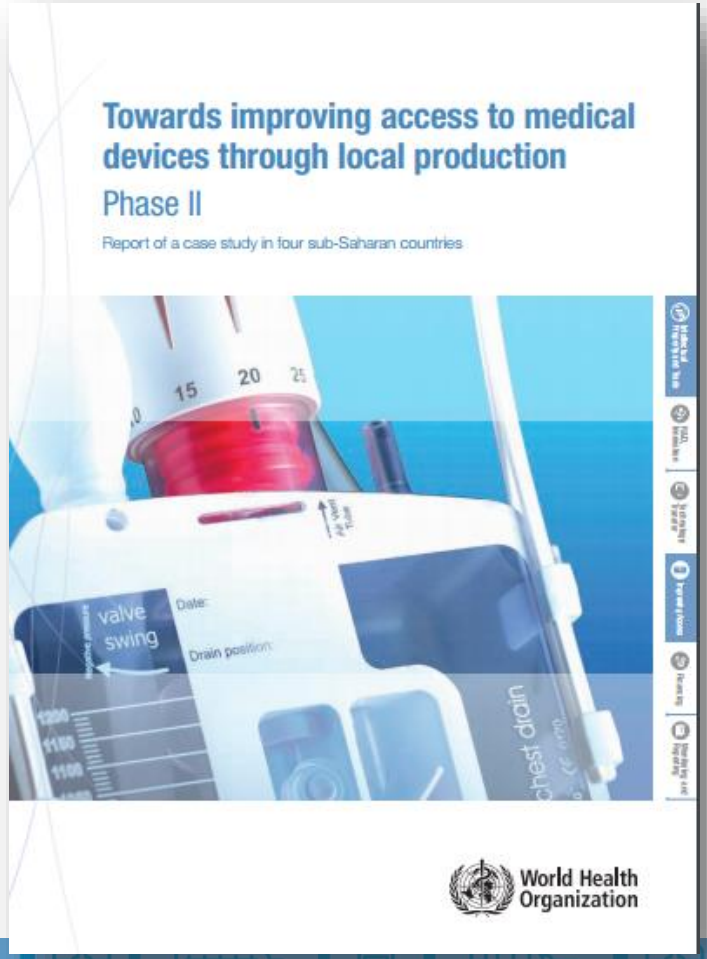
Innovation

- GOALS: represent tests that should be reasonably available for people who need them, regardless of the setting
- facilitate group purchasing to reduce costs
- inspire development of logistical solutions for laboratory testing in resource-poor settings

- clarify priorities for policymakers
- encourage setting common goals regarding laboratory testing

- OUTCOME: paving the way toward improved health care delivery and ultimately better patient outcomes

Innovation


Towards improving access to medical devices through local production
Phase II
Report of a case study in four sub-Saharan countries
valve swing
Date:
Drain position:
chest drain
World Health Organization

Regulation – Norms and Standards

WHO Expert Committee on Biological Standardization (ECBS)

WHO Collaborating Centers

GOAL

- development of internationally recognized norms, standards and guidelines, including biological reference material
- WHO Manual for the establishment of Secondary Standards

Regulatory system strengthening

GOAL: Assessments of national regulatory systems

- Reviews aim at strengthening national regulatory and control capacity through an assessment of the situation, the identification of specific needs, and the provision of appropriate technical support and training.
- review the existing legal framework, regulations and control activities with regard to medicinal products and medical devices in order to assess the national regulatory capacity against a set of predefined parameters;
- in collaboration with national officials, identify gaps and develop strategies to address these gaps;
- identify specific areas and activities for WHO’ s technical input.

Regulation - Prequalification

Vision: good-quality health products for everyone.

Mission: to ensure timely availability of quality-assured health products for the prevention, diagnosis and treatment of priority diseases, through the assessment of the quality, safety and efficacy/performance of these products, with a focus on their suitability for use in resource-limited settings.

Regulation - Prequalification

PQDx Scope

- HIV (RDTs, NAT qual and quant)
- HCV (RDTs, EIAs, NAT)
- Malaria RDTs
- G6PD deficiency IVDs
- HBsAg RDTs
- CD4 POC IVDs
- HPV POC IVDs

PQ: Training to Regulators and Industry

- China
- India
- South Africa (Early infant diagnosis)
- Russia

PQ Harmonisation and Capacity Building Activities

- IMDRF
  - MC (Observer status)
  - MDSAP
  - GRRP
  - Adverse Event Terminology
  - Common Data Elements
- AHWP
  - General support
  - Request for assistance with WHO guidance

PQ Harmonisation and Capacity Building Activities

- Pan African Harmonisation Working Party
  - General support
- ALADDIV
  - Training at general meeting
- AIDS 2016/ ASLM 2016
  - HIV self testing etc
- ISO
  - ISO 20916: In vitro diagnostic medical devices — Clinical performance studies using specimens from human subjects – Good study practices

PQ Guidance

1. TECHNICAL GUIDANCE SERIES FOR WHO PREQUALIFICATION		
The Prequalification Team – Diagnostics is developing a Technical,Guidance Series for manufacturers interested in WHO prequalification of,their IVD and will assist manufacturers in meeting prequalification,requirements. It should be read in conjunction with relevant,international and national standards and guidance.		
TGS 1	Standards applicable to the WHO Prequalification of in vitro diagnostics	
TGS 2	Establishing stability of an in vitro diagnostics for the WHO Prequalification	**Comment period closed**
TGS 3	Principles of performance studies	**Comment period closed**

http://www.who.int/diagnostics_laboratory/guidance/en/

PQ Guidance

2. SAMPLE PRODUCT DOSSIER FOR WHO PREQUALIFICATION	
The Prequalification Team – Diagnostics have prepared sample product,dossiers based on a fictitious IVD to provide manufacturers with an,example of the type of information that may be included in a product,dossier submitted to WHO Prequalification.	
Sample Product,Dossier for a CD4 IVD	
Sample Product Dossier for an IVD intended,for HIV self-testing	Comment period closed
Sample Product Dossier for a Qualitative,Nucleic Acid Test to detect HIV-1 and HIV-2	Comment period closed
Sample Product Dossier for a Quantitative,Nucleic Acid Test to detect HIV-1 RNA	**NEW**

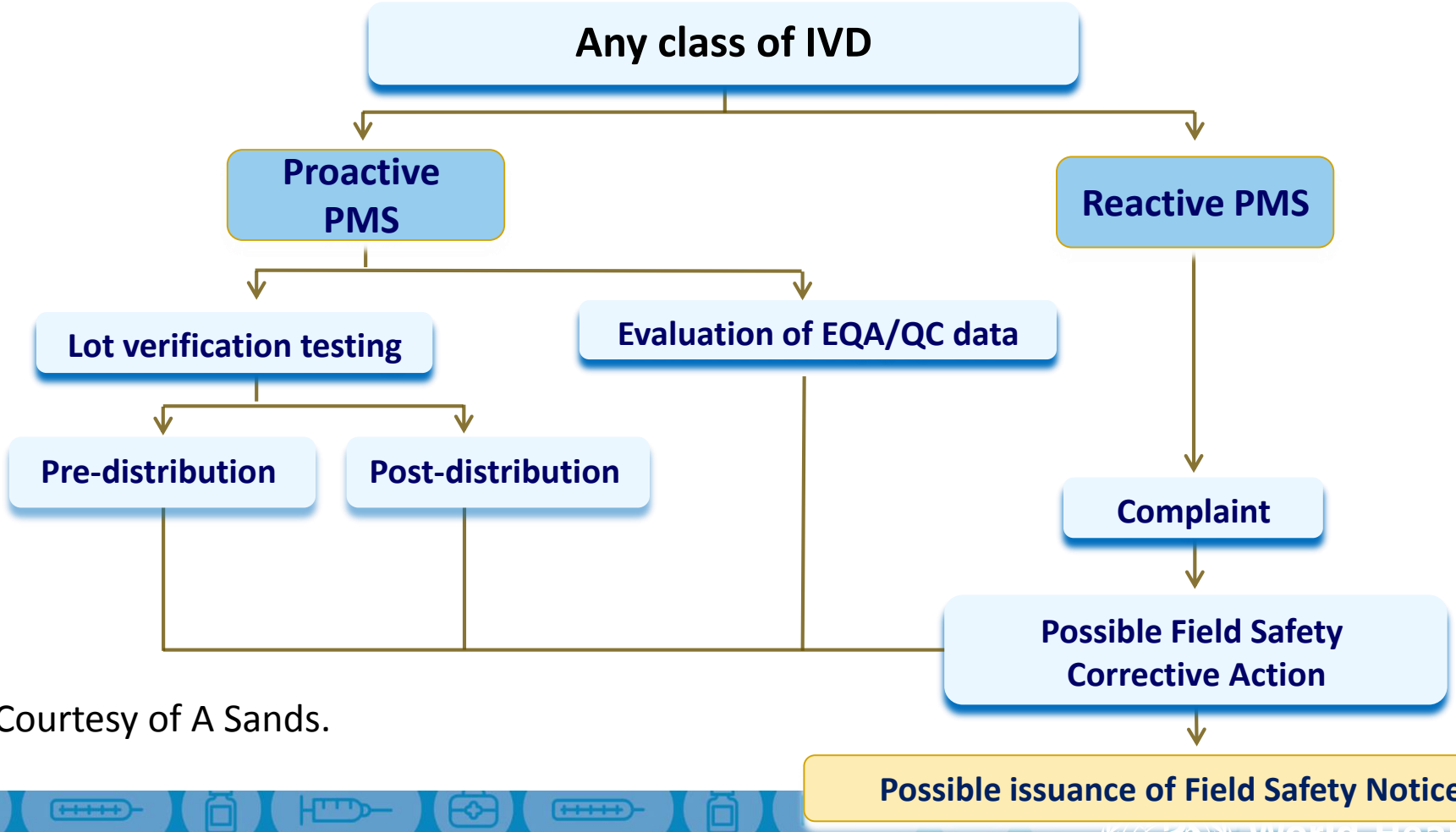
PQ Guidance

3. TECHNICAL SPECIFICATION SERIES FOR WHO PREQUALIFICATION		
The Prequalification Team – Diagnostics is developing a Technical,Specification Series for manufacturers interested in WHO,prequalification of their in vitro diagnostic medical device (IVD). This series will set out appropriate,performance evaluation criteria to meet PQ requirements.		
TSS 1	Technical specifications for WHO prequalification of HIV rapid diagnostic tests for professional use and/or self-testing	Comment period closed
TSS 2	Technical specifications for WHO prequalification of IVD medical devices to identify Glucose-6-phosphate dehydrogenase (G6PD) activity	**NEW**

PQ Guidance

Aspect	Testing requirements	Comments	References
Precision of measurement			
Repeatability, reproducibility	Both repeatability (within-condition[1]) and reproducibility (between-condition[1]) estimated using panels of at least: • 1 analyte-negative specimen • 1 low reactivity positive specimen (near assay cut-off) • 1 medium reactivity positive Each panel member tested: • in five replicates, • using 3 different lots, • over 5 days (not necessarily consecutive) with one run in that day (alternating morning/afternoon), and • at each of at 3 different testing sites The effect of operator-to-operator variation on IVD performance is to be included as part of the precision studies (see also Comment 8). Testing should be done: • by personnel representative of expected end users , comprising subjects not trained in the use of the IVD • unassisted • using *only* those materials provided with the IVD (e.g. IFU, labels and other instructional materials). Users should be selected based on a pre-determined and contextually appropriate level of education, literacy and auxiliary skills that will challenge the usability of the IVD and reflect the diversity of intended users and operational settings.	1. E.g. within- or between-run, -lot, -day, -operator, -site, etc. 2. Precision must be determined for each pathogen and/or analyte for which detection is claimed (e.g. HIV-1 Group M or HIV-1 Group O antibody, HIV-2 antibody, HIV-1 p24 antigen , etc., as appropriate). Similarly for IVDs that include a claim for detection of HIV Ag, appropriate specimens must be included in the precision testing panel. 3. Ideally, the testing panel should be composed of natural (i.e. undiluted) specimens. Where this is not feasible, stock specimens that are to be diluted should represent a range of stages of infection (antibody maturation) in order to take into account the limitations of mimicking low IVD reactivity with a high avidity specimen. 4. IVDs which include whole blood as a specimen type must include evidence of precision in at least spiked whole blood specimens (negative whole blood spiked with high-titre positive plasma/serum specimens). 5. The testing panel should be the same for all operators, lots and sites. 6. Master lots should be composed of different batches of critical components. 7. Results must be statistically analysed by ANOVA to identify and isolate the sources and extent of any variance. 8. The effect of operator-to-operator variation on IVD performance is also to be considered as a human factor when designing robustness (flex) studies (see page 15).	CLSI EP05-A3 [3] ISO 13612:2002 [4]

WHO post-market surveillance of IVDs



Courtesy of A Sands.

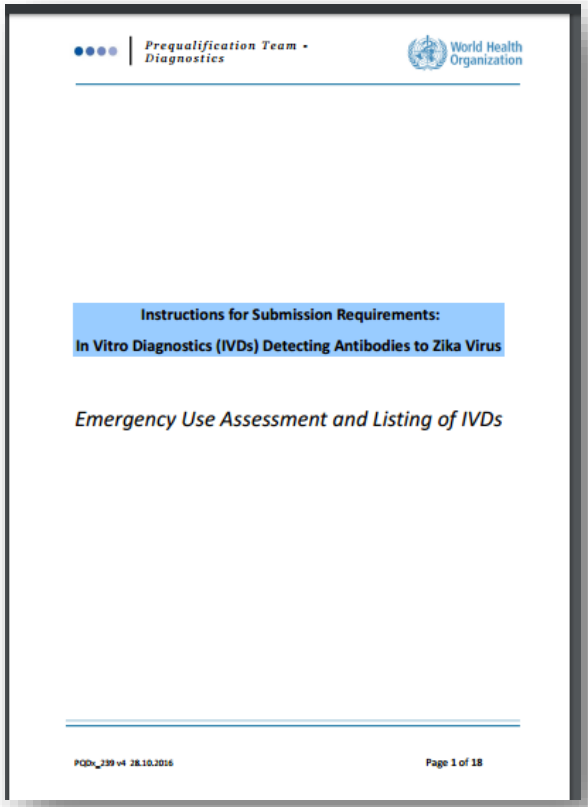
Blueprint

- **List 1**: Crimean Congo haemorrhagic fever, Ebola virus disease and Marburg, Lassa fever, MERS and SARS coronavirus diseases, Nipah and Rift Valley fever.
- **List 2**: chikungunya, severe fever with thrombocytopaenia syndrome, and Zika virus

PHEIC Zika Virus

- Target product profile
- IVD landscape analysis
- Emergency use assessment and listing procedure
- Development of ZIKV biological reference material
- Regulatory pathways
- Biobanking

PHEIC: Zika virus EUAL


Prequalification Team - Diagnostics

World Health Organization

Instructions for Submission Requirements:

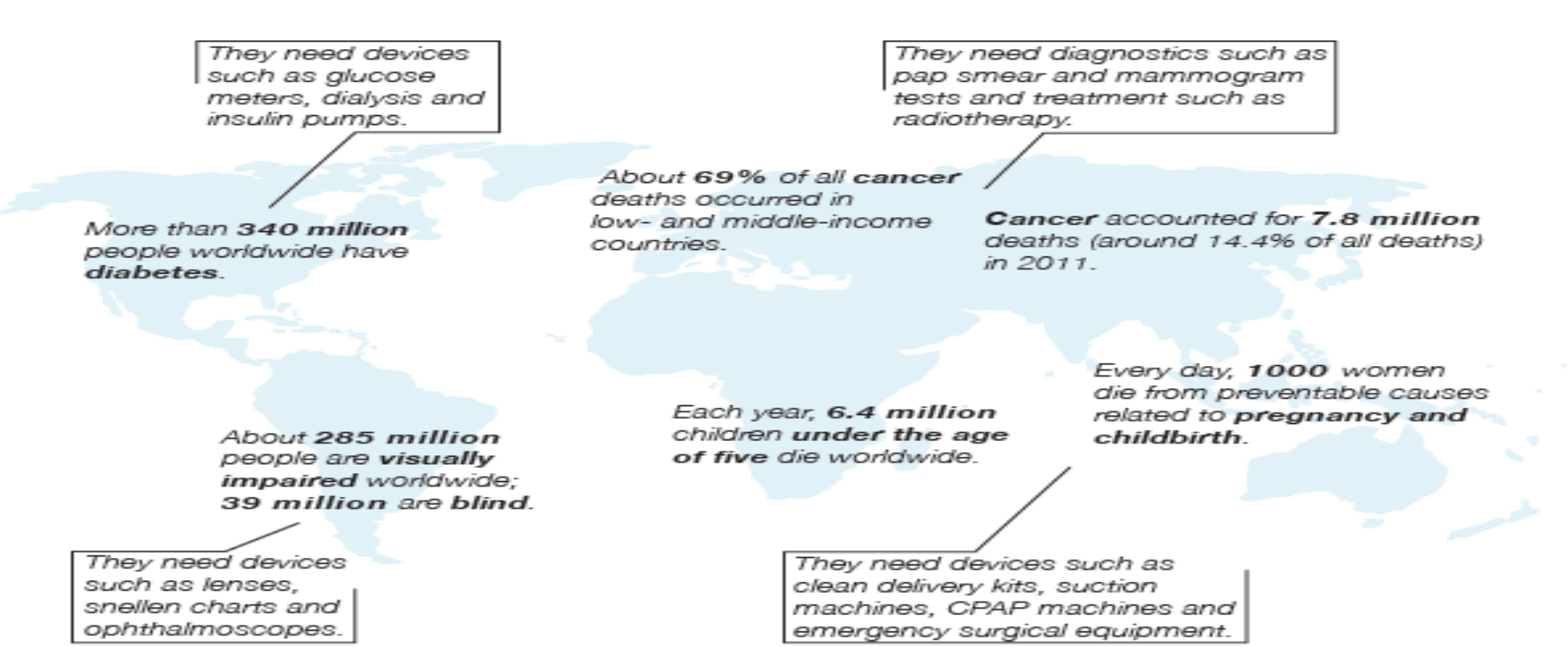
In Vitro Diagnostics (IVDs) Detecting Antibodies to Zika Virus

Emergency Use Assessment and Listing of IVDs

PQDx_239 v4 28.10.2016

Page 1 of 18

- **step 1**: review of the manufacturer's QMS documentation;
- **step 2**: review of the documentary evidence of safety and performance, including labelling and product performance specifications, and associated verification and validation studies;
- **step 3**: performance evaluation of limited scope to verify critical analytical and clinical performance characteristics.



Medical devices should be available to everyone. Everywhere.
But where they are most needed, they are least available.

43 low- and middle-income countries do not even have at least an average of 1 district hospital per 1 000 000 inhabitants.

24 low-income countries do not have a single computed tomography (CT) per 1 000 000 inhabitants and 8 out of 134 countries have no CT scanners at all.

Low- and middle-income countries face significant challenges such as:

- *Limited financial resources*
- *Lack of available information*
- *Lack of training*
- *Inappropriate donations*
- *Fragmented health services*
- *Shortage of biomedical engineers*

How to say 'thank you' in 28 languages

Special thanks to S Hill, M Ward, I Prat, J Hansen, A Velasquez