Word Health Organization Update

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With thanks to Josée Hansen for her contribution

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Presentation Layout

- Prequalification of IVDs
- Model Regulatory Framework for medical devices
- WHO NRA assessment tool

PREQUALIFICATION OF IN VITRO DIAGNOSTICS PROGRAMME

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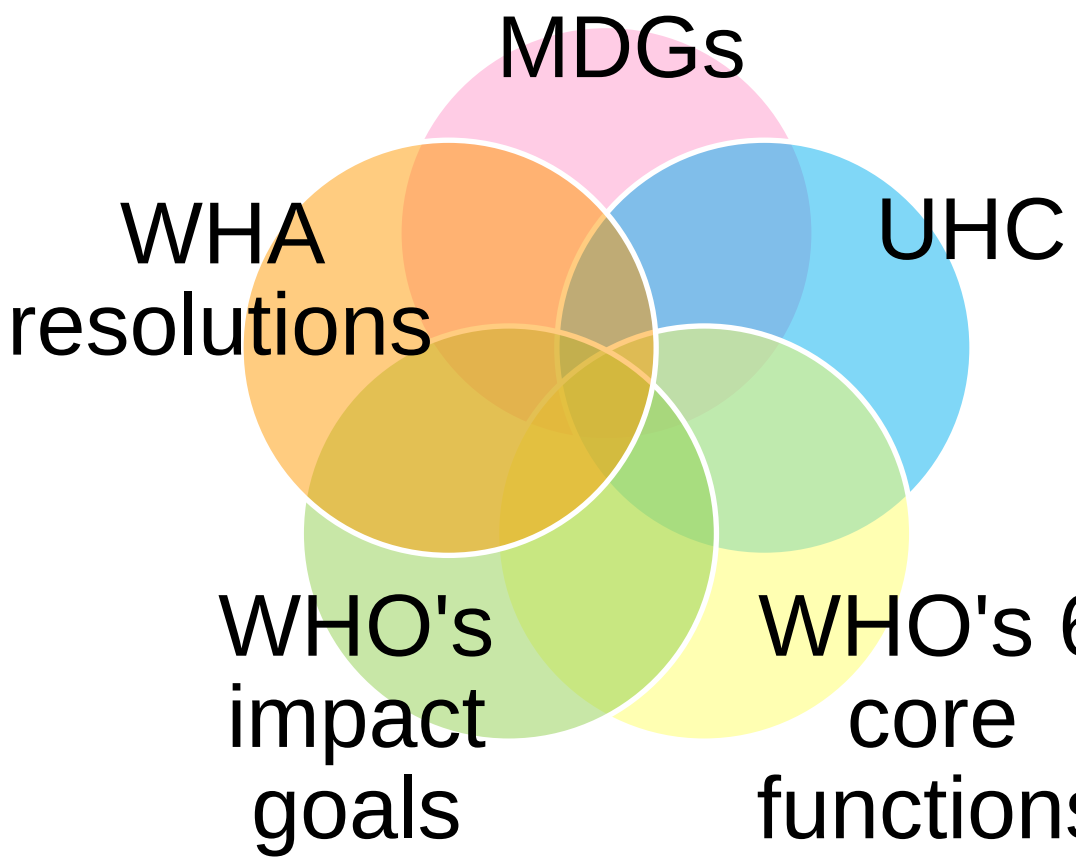
WHO's work in IVDs area: background



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Millennium development goals

The United Nations Millennium Development Goals are eight goals that all 191 UN Member States have agreed to try to achieve by the year 2015.

4. to reduce child mortality;

5. to improve maternal health;

6. to combat HIV/AIDS, malaria, and other diseases;

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Universal health coverage

Universal coverage is based on the WHO constitution of 1948 declaring health a fundamental human right and on the Health for All agenda set by the Alma-Ata declaration in 1978.

For a community or country to achieve universal health coverage, several factors must be in place, including:

Access to essential medicines and technologies to diagnose and treat medical problems.

Role of WHO prequalification

- Facilitate access to safe, appropriate priority IVDs, medicines and vaccines

- Support two of WHO's six core functions
  - setting norms & standard/promoting their implementation
  - providing technical support, catalyzing change & building institutional capacity

- Contribute to achieving four of WHO's impact goals
  - reduce under-five mortality
  - reduce maternal mortality
  - reduce the number of people dying from AIDS, tuberculosis and malaria
  - eradicate polio

Prequalification of in vitro diagnostics programme

- Includes three components:
  - Review of a product dossier;
  - Performance evaluation, including operational characteristics; and
  - Manufacturing site(s) inspection.

- Looks into quality, safety and performance through dossier review, performance evaluation and inspection
  - Dossier: safety and performance
  - Performance evaluation: performance
  - Inspections: quality

Reference documents

PQDx is aligned with best international practice for IVDs

- ISO (and EN) standards: QMS, risk mgt, stability, labelling, perf. evaluations, etc.
- GHTF/IMDRF guidance: STED, MDSAP, labelling, EPs, PMS
- CLSI guidance: stability, V&V,
- NRAs: FDA, EU

What does PQ do differently to GHTF/IMDRF

Requirements are based on the same set of standards – PQ is aligned with internationally accepted practice BUT

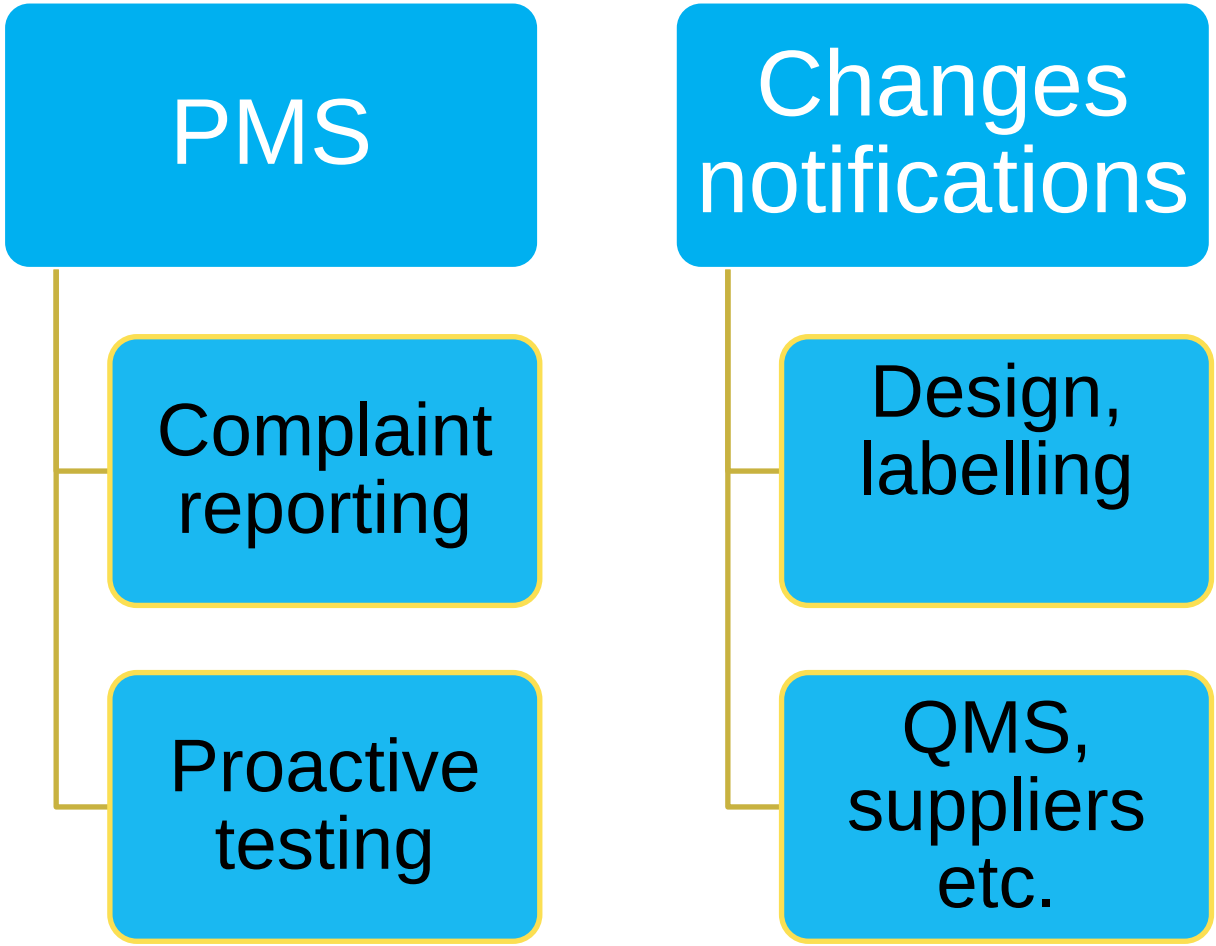
Assess products' regulatory versions intended for the global market

- Where a stringently reviewed versions exist, they are often not supplied to the global market – RoW versions differ from stringently assessed version in Mx site, QC, labelling, key suppliers, composition, intended use etc.

Review aspects of particular relevance for resource-limited settings

- Risk assessment, stability, flex studies, labelling, training and support network
- Take into account environment and user skills

Post-prequalification phase



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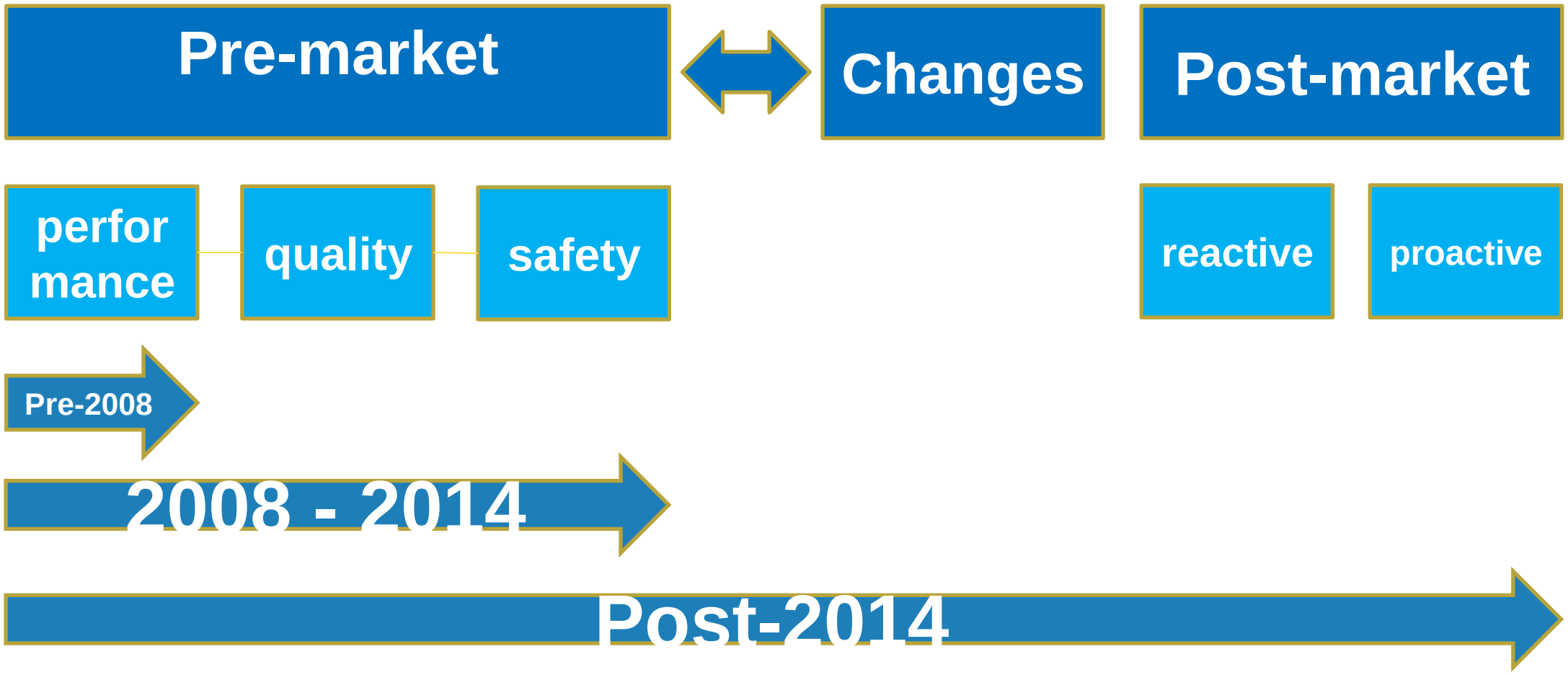
PQ in a regulatory framework



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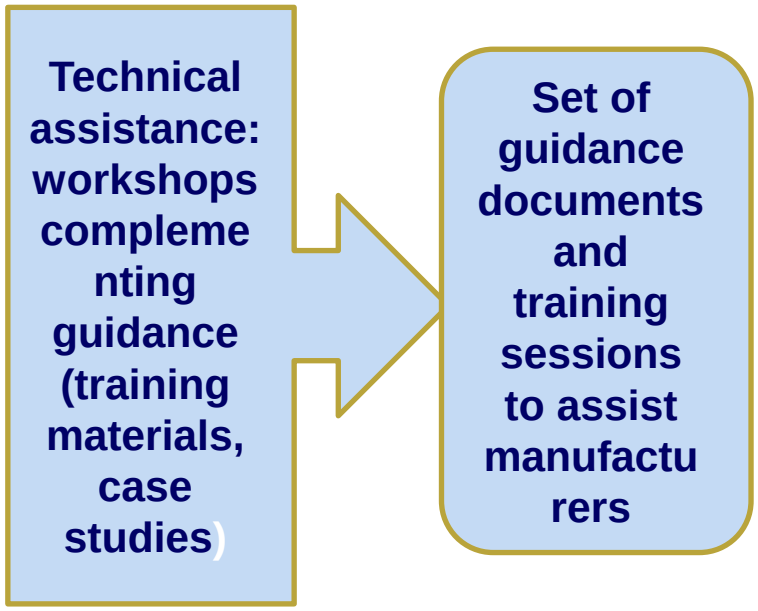
Future developments

- Product dossier:
  - 3 sample dossiers (VL, EID and HIVST)
  - several guidance documents to support dossier submissions
    - TGS1 Reference documents
    - TGS2 Stability studies
    - TGS3 Principles for performance studies
    - TGS4 Sample dossiers
    - TGS5 Product specific guidance
    - TGS6 IFU
    - TGS7 Flex studies
    - TGS8 Specimen types
    - TGS9 Test method validation
  - IMDRF ToC (more granularity than STED)
- Inspections:
  - guidance documents
    - TGS10 Quality control principles
    - TGS11 Outsourcing and supplier mgt



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Prequalification of in vitro diagnostics programme

- Lab evaluations:
  - WHO has been supporting studies through WHO collaborating labs;
  - new mechanism being designed to capture efforts from various partners and join forces with other organizations supporting IVDs QA
- Joint assessments
  - Capacity building mechanism to strengthen NRAs and provide insight into PQDx assessment
  - Sessions for regulators
- PQ framework expansion to HPV
- Collaborative procedure

MODEL REGULATORY FRAMEWORK

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Purpose

- A Model Regulatory Framework for medical devices including IVD's with global input and reflecting a modular approach in regulating medical devices
  - How to begin regulating?
  - What to regulate: harmonized definitions and guiding principles
  - How to regulate; stepwise development and implementation
  - When to regulate: stepwise approach
- Regional workshops and capacity building
- Parallel to the NRA assessment tool for medical devices

Justification

- Medical products should be safe and effective
- Resolution WHA 67.20 on Regulatory System Strengthening for medical products
- Member states request for support on regulatory system strengthening
- Increasing importance of medical devices: regulating an existing market
- Globalizing world
- Lack of regulation in many member states

(http://apps.who.int/medicinedocs/documents/s21456en/s21456en.pdf)

Publications

- A Model Regulatory Program for Medical Devices: An International Guide 2001 PAHO
- Medical Device Regulations: Global overview and guiding principles 2003 WHO
- The GHTF Regulatory Model 2011
- AHWP Playbook for implementation of medical device regulatory frameworks 2014

What's new?

- Working group is engaged in the development of the Model Regulatory Framework for medical devices
- Public consultations to generate feedback and input
- Adoption by Expert Committees

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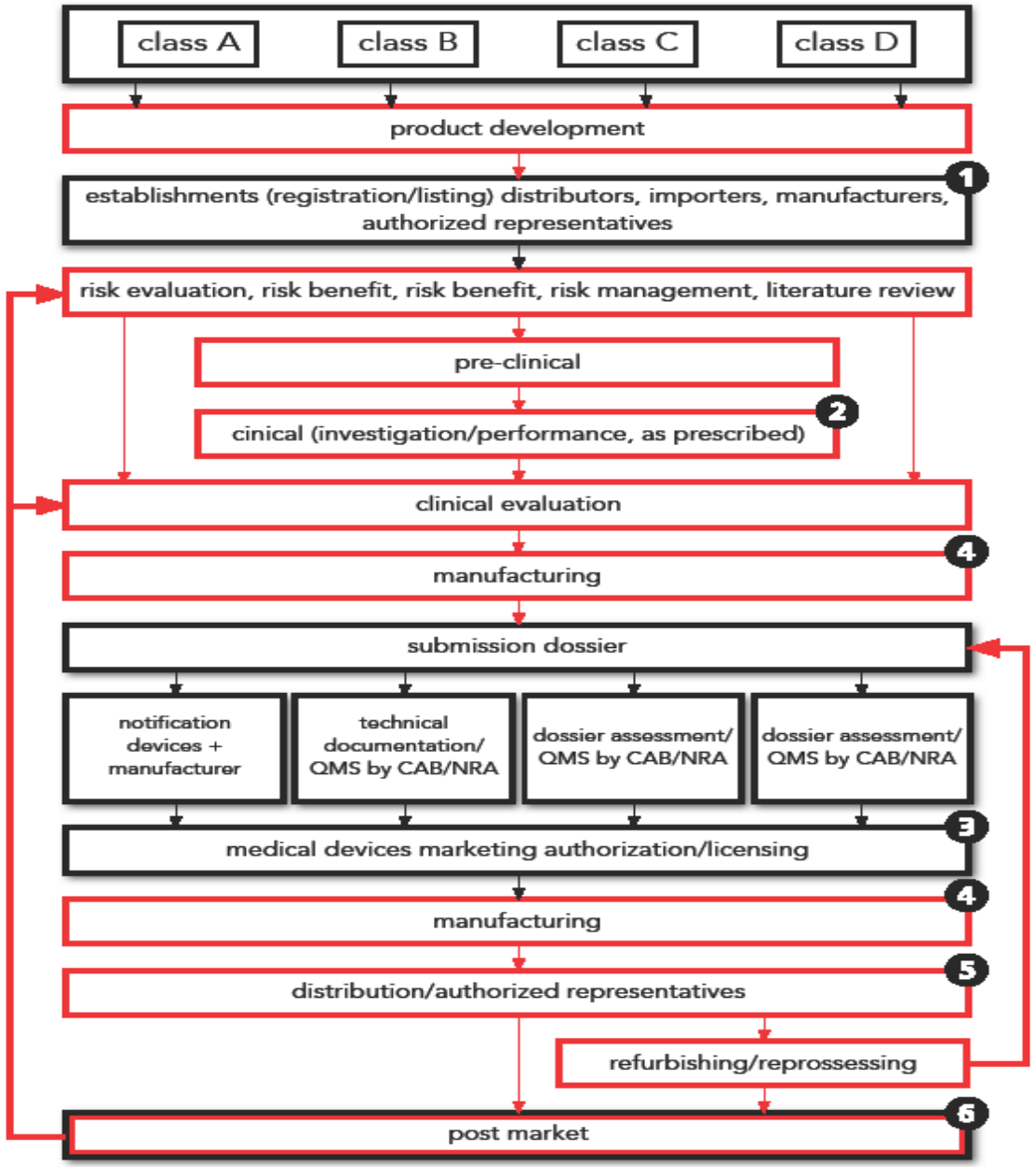
Where we are now

- Definition of a medical device and IVD as a medical device
  - GHTF definitions
- Life cycle of a medical device
- Stepwise approach: three levels



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Stepwise Approach

Basic Elements

- Establishment of Essential Principles of Safety and Performance
- Issuing guidance documents on regulatory requirements
- Registration of manufacturers, importers and distributors
- Listing of medical devices placed on the market
- Import controls
- Market surveillance, supply chain control, traceability
- Labelling and instruction for use controls
- Serious adverse events, recalls, FSCAs or withdrawal from market in exchange with other NRAs
- Provision for exemptions from regulatory requirements e.g. donations and humanitarian use.
- Enforce regulations

Stepwise Approach

Intermediate Elements

- QMS including good record keeping requirements
- Administrative controls for reliance
- Recognition and adoption of international standards
- Control of advertising
- Adverse event reporting within a vigilance system*

Full Implementation

- Premarket decision on compliance of medical device with essential principles (with reliance and/or review)
- Notification of clinical investigations and/or serious deviations and/or adverse events
- QMS auditing (by reliance and/or by auditing)
- Appoint and oversee CABs
- Establishment of a test laboratory function (national or regional or by reliance)
- Mechanism for analyses and dissemination of alerts on medical devices (national, regional, international)

NRA ASSESSMENT TOOL

Objective of NRA assessment

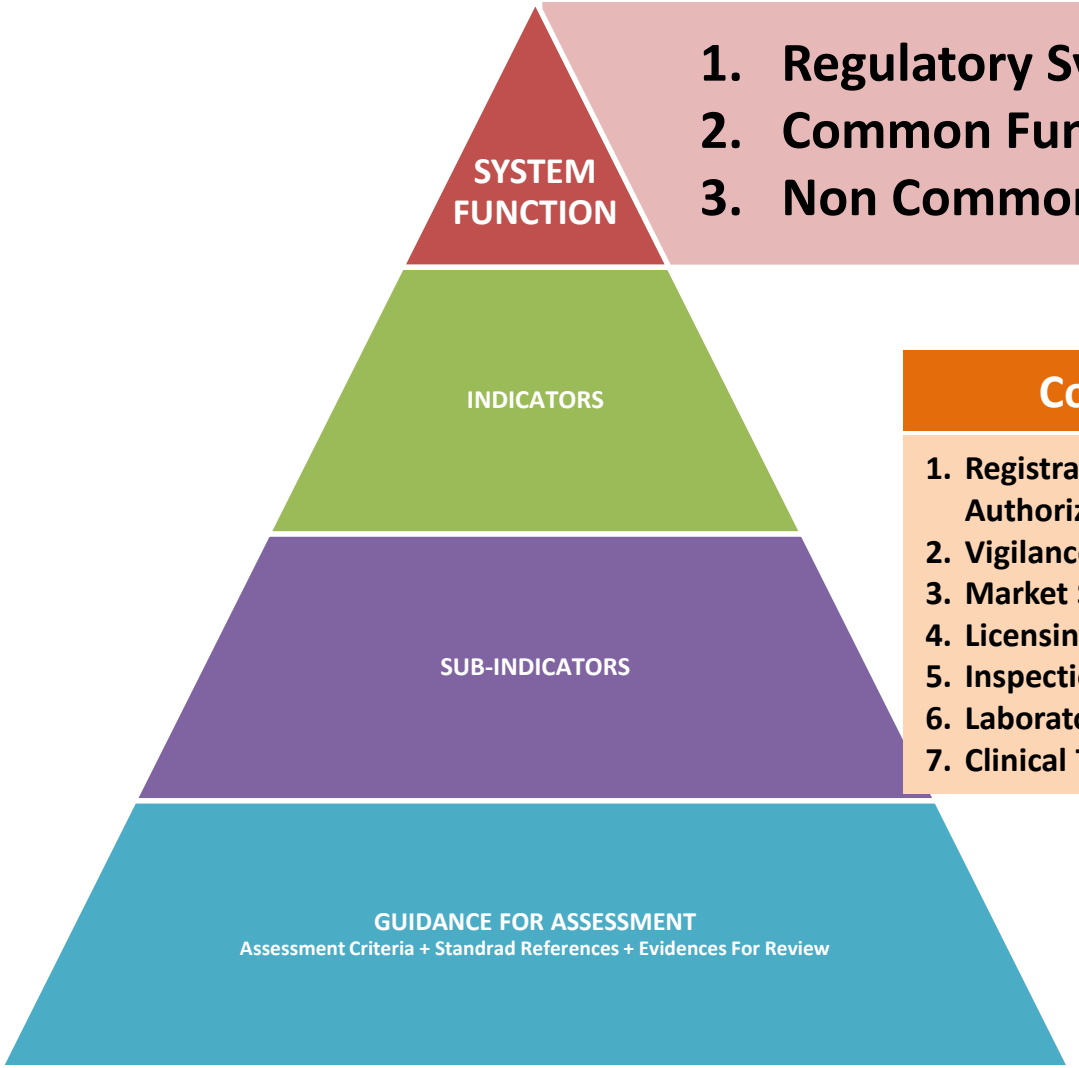
Strengthen the regulatory *systems* for all medical products to assure the quality, safety and efficacy of all medical products

History

- Vaccines since 1997
  - NRAs assessed
- Medicines since 2001
  - NRAs assessed
- Medical devices
  - WHO NRA tool for medical devices developed 2013.
  - PAHO tool for medical devices: 2012-2015. Piloted in 5 countries

WHO Global Assessment Tool 2015

National Regulatory System (NRS) and Functions (NRF)



1. Regulatory System
2. Common Function
3. Non Common Functions

Common Function	Non Common Function
1. Registration & Marketing Authorization	1. Lot Release
2. Vigilance	2. Registration of health personnel
3. Market Surveillance and Control	3. Control of Promotion and advertisement
4. Licensing	4. Control of Narcotics, Psychotropic Substances and precursors
5. Inspection & Enforcement	5. Audit of Conformity assessment bodies
6. Laboratory Access & Testing	
7. Clinical Trial Oversight	

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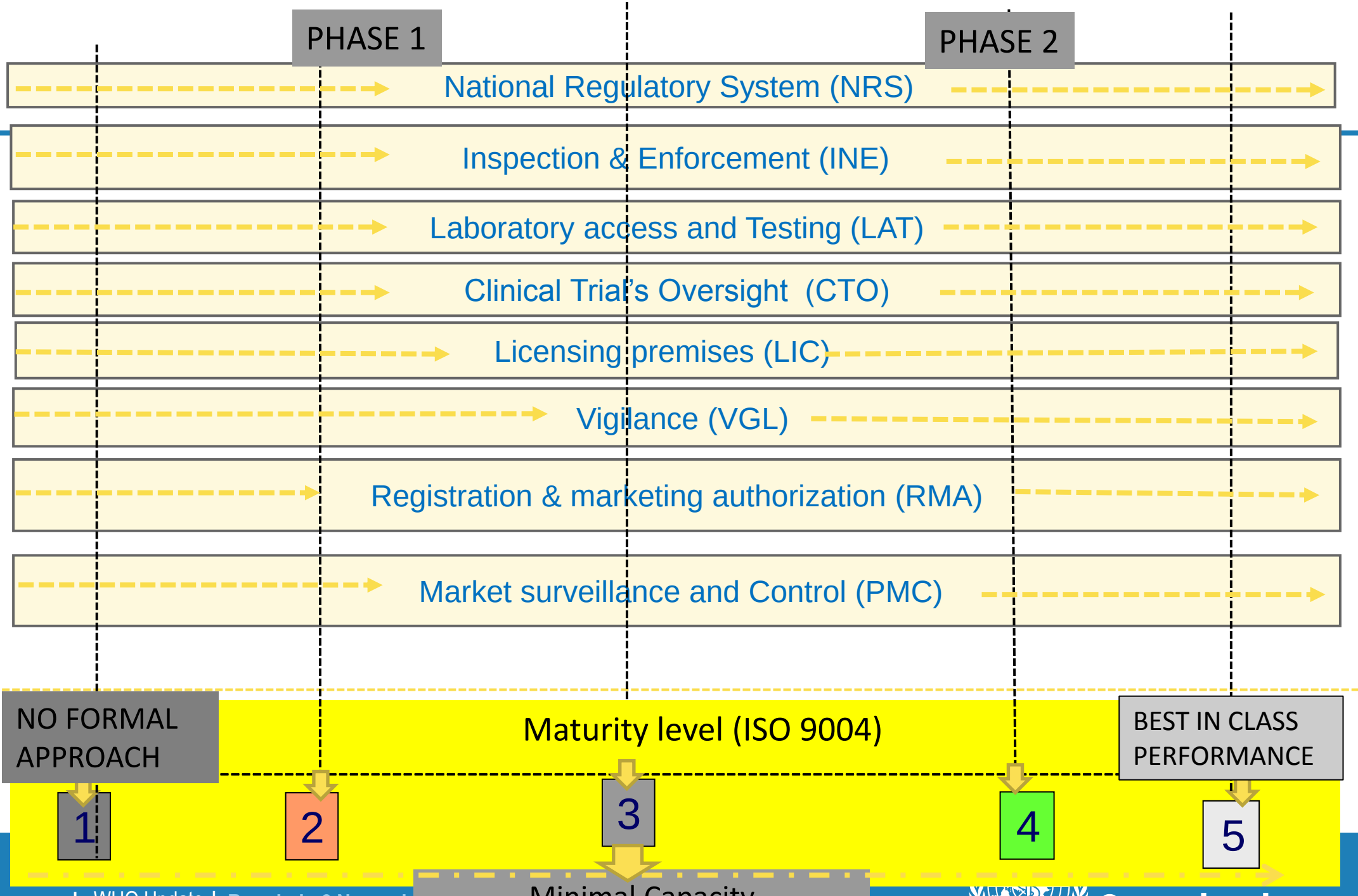
Harmonized tool : Phase 1 and 2



Policy for NRA Assessment medical devices

- Focus on member states with no or limited regulatory system for medical devices in place
- Focus on basic level of regulation
- Some basic regulatory system has to be in place

Next steps and time line

- First draft of the Model Regulatory Framework for medical devices January 2015
- Public Consultations in April and August
- In parallel: regional awareness workshops
- Under development: self assessments and capacity building for regulating medical devices at basic level
- In parallel: NRA assessment if applicable

Thank you very much for your attention.

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