Regulatory Convergence: Where are we Heading?

ALADDIV Vth International Workshop: Accessible and Quality Assured In Vitro Diagnostic Tests for Public Health Programs

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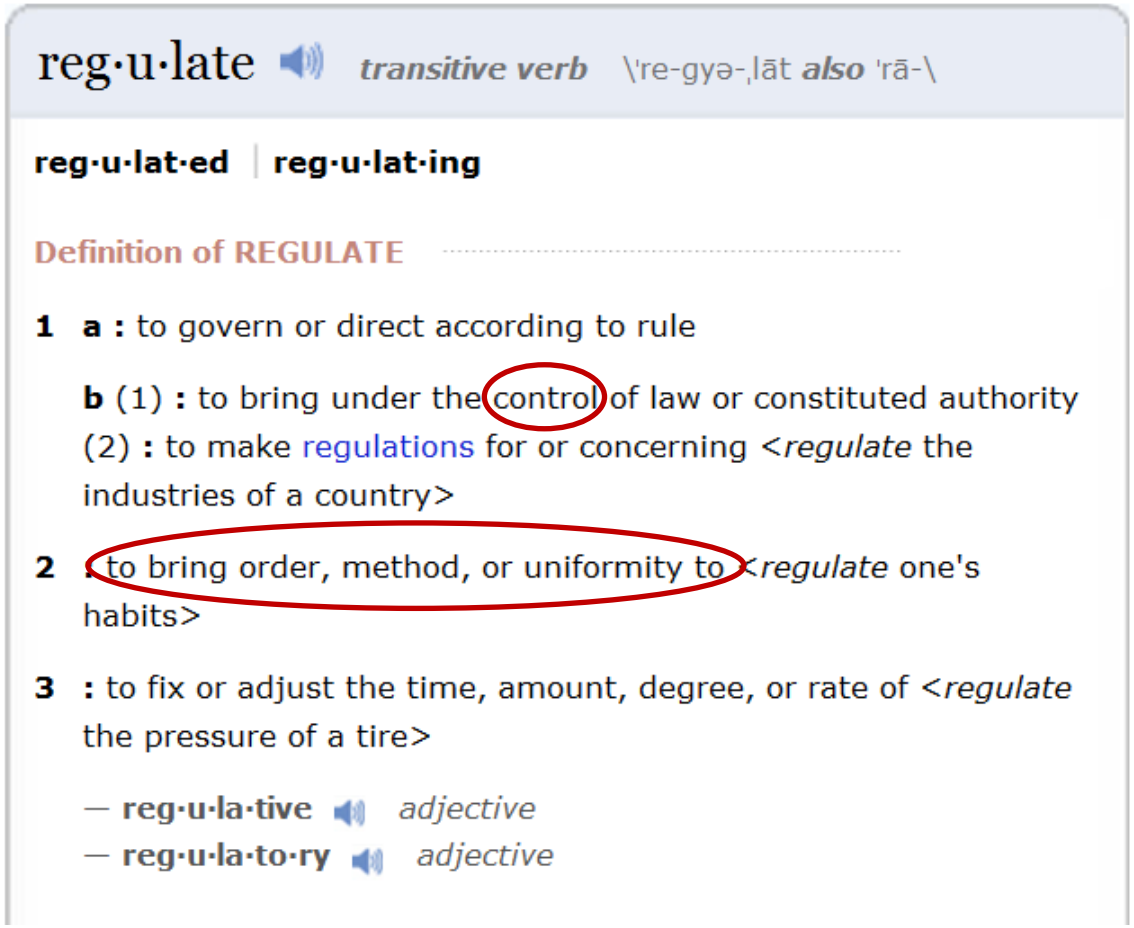
To be Covered

- What is regulation?
- Critical issues to be addressed in IVD assessment
- Best practice assessment principles
- The role of risk classification in IVD assessment
- The role of global standards
- Harmonization vs. Convergence

What does it mean to regulate?



reg·u·late *transitive verb* \'re-gyə-ˌlāt *also* 'rā-\

reg·u·lat·ed | **reg·u·lat·ing**

Definition of REGULATE

1 **a :** to govern or direct according to rule

b (1) **:** to bring under the control of law or constituted authority (2) **:** to make regulations for or concerning <*regulate* the industries of a country>

2 **:** to bring order, method, or uniformity to <*regulate* one's habits>

3 **:** to fix or adjust the time, amount, degree, or rate of <*regulate* the pressure of a tire>

— **reg·u·la·tive** *adjective*
— **reg·u·la·to·ry** *adjective*

Where we want to be…

Have tests that are:

REGULATION

Reliable – always work

Accurate – provide a correct result

Robust – compatible with extreme working and storage conditions

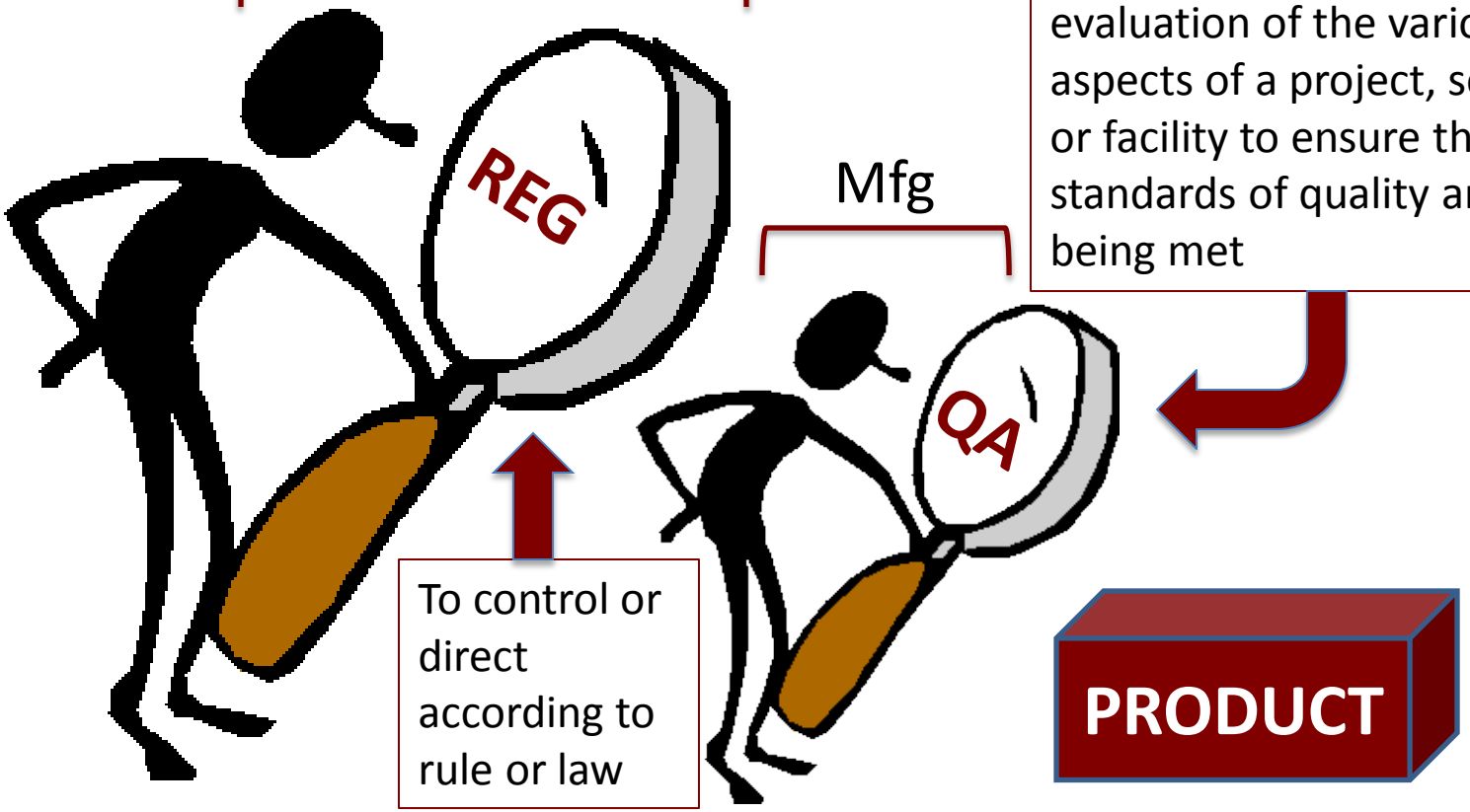
ACCESS

Affordable – to meet budget constraints

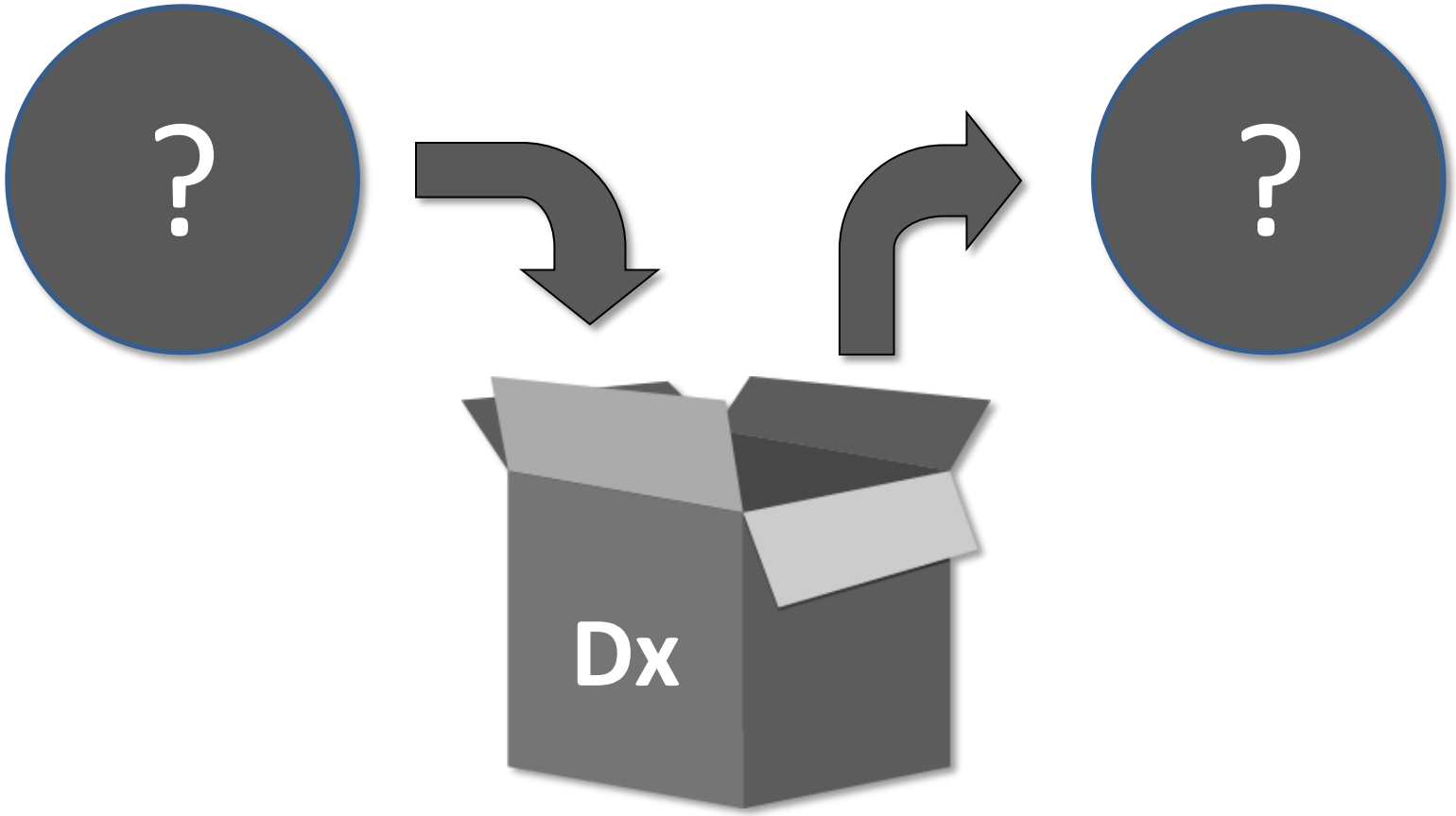
Available – in sufficient supply to meet demand

Compatible – appropriate for the population with which it will be used

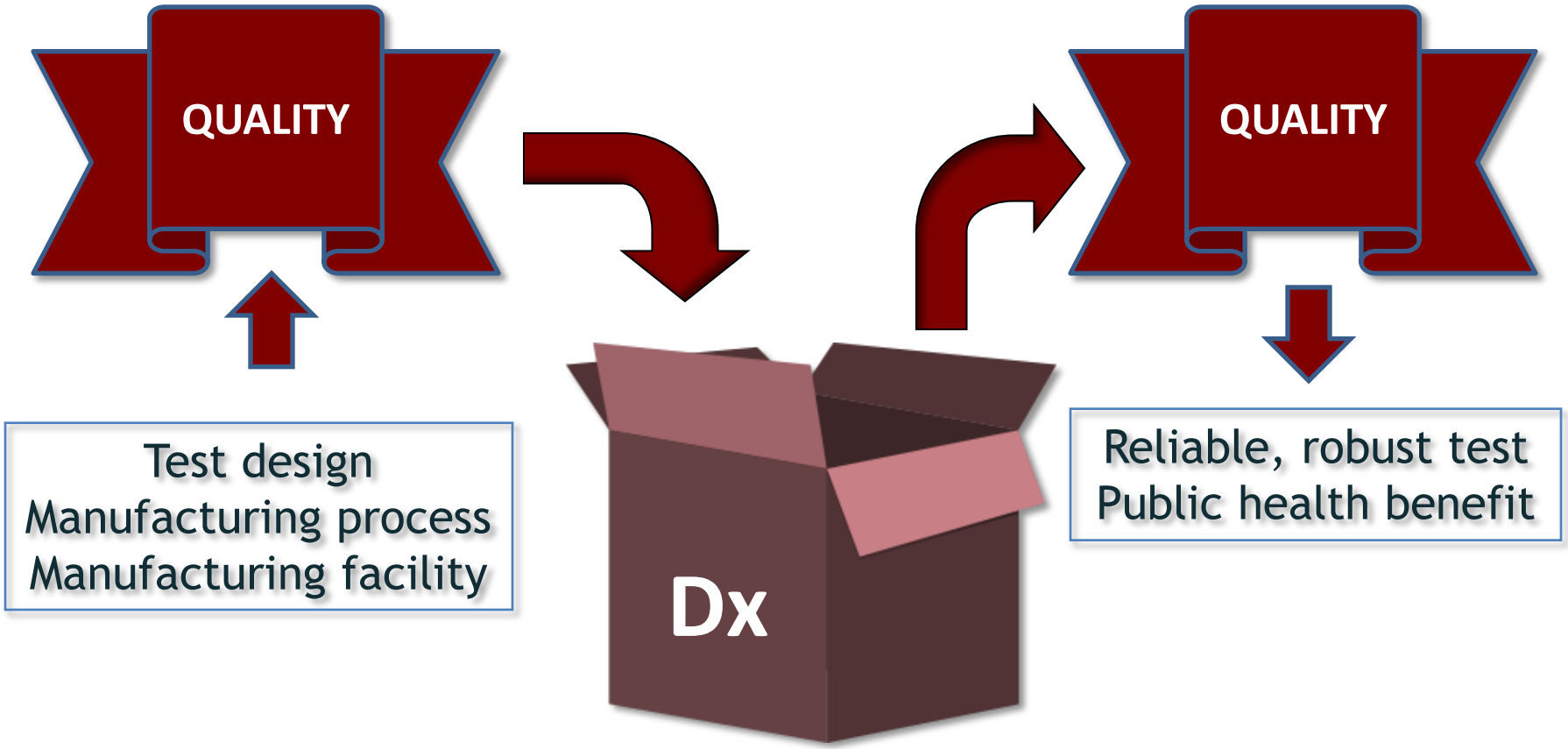
Regulation and Quality Assurance



Out of Control



In Control


QUALITY
QUALITY
Test design
Manufacturing process
Manufacturing facility
Dx
Reliable, robust test
Public health benefit

What is the purpose of regulation?

nsure that products are safe and effective for their intended use.

valuate evidence to support claims.

nforce the regulations.

General IVD Assessment Concepts

1. The IVD must meet accepted levels of safety and performance (or, in some contexts, referred to as effectiveness)

General IVD Assessment Concepts

2. Safety and performance of IVDs can be assessed through a balance of:
   - Premarket scrutiny
   - Adequate manufacturer quality management systems (QMS)
   - Implementation of effective post-market surveillance (PMS)
     - Active vs. passive

General IVD Assessment Concepts

3. Risk classification provides a rational approach to the assessment process.
   - Many IVDs, limited resources
   - Increased risk = Increased oversight
   - Public health risk vs. individual health risk
   - Risk classification may differ depending upon intended use setting

General IVD Assessment Concepts

4. Assessment bodies are most effective when there are consequences that discourage inappropriate activity.

Applying Regulations: Enforcement

QA → PRODUCT →

- Consistent performance
- Trust in results
- Public health benefit
- Optimized use of resources

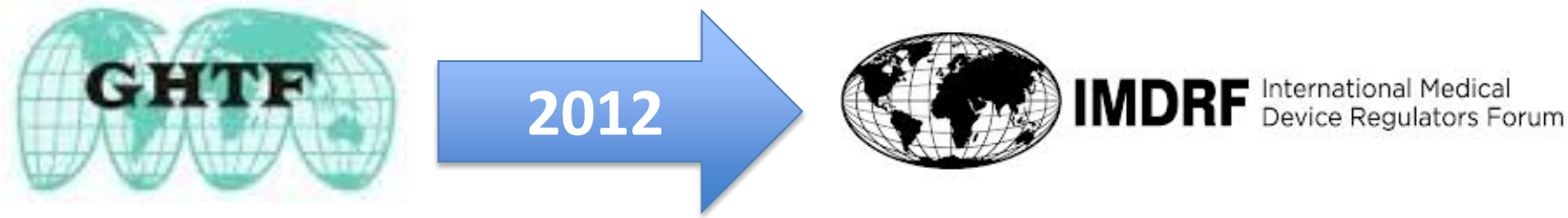
DISINCENTIVES
CONSEQUENCES

REGULATIONS →

Legal action
Removal from list
Etc.

Best Practice Assessment Principles

- Global Harmonization Task Force (GHTF)
  - Founded in 1992
  - Group of representatives from global national medical device regulatory authorities (US, Canada, Japan and Australia) and from industry
  - Purpose: Convergence of regulatory practice and identification of best regulatory practice
  - Publication of documents



GHTF: Premarket Scrutiny

- Essential Principles of Safety and Performance of Medical Devices (GHTF/SG1/N68:2012)
  - When followed, would provide assurance that the product is safe and performs as expected
  - IVD assessment bodies generally accept these principles and address them in their evaluations
  - Seeking conformity to Essential Principles

GHTF: Premarket Scrutiny, cont.

- Summary Technical Documentation (STED)
  - For premarket assessment of the IVD
- Contents of STED
  - Device description
  - Essential Principles checklist
  - Risk analysis and control summary
  - Design and manufacturing information
  - Product verification and validation (performance studies)
  - Labeling

GHTF: QMS

- Manufacturer should have a functional QMS that is based on internationally recognized standards
- QMS requirements vary according to risk classification of the IVD
- QMS may be audited for continued compliance after product is approved
- IMDRF effort to harmonize QMS auditing
  - Medical Device Single Audit Program (MDSAP)

GHTF: PMS

- Manufacturer is expected to implement, through its QMS, a process to evaluate the continued conformity of its IVD to the Essential Principles, including:
  - Complaint handling
  - Vigilance reporting
  - Corrective and preventive action

GHTF: Risk Classification

- Role of IVDs demands that they be of high quality
- However, not feasible that all IVDs be assessed in the same manner
  - Vast number of products for a very broad range of analytes
  - Limited resources available to conduct assessments
- Use of a risk-based approach for the assessment of IVDs

GHTF: Risk Classification, cont.

- GHTF created risk classification rules* to determine the level of premarket regulatory assessment required for an IVD
  - Considered sufficient for each risk class to safeguard the health and safety of patients, users, and others

** GHTF/SG1/N045:2008 "Principles of In Vitro Diagnostic (IVD) Medical Devices Classification"*

GHTF Risk-Based Approach

- Classify IVDs according to the risk they pose to personal and public health
- Take into account potential outcomes if the test does not perform properly or is not available
- Risk class determines the level of scrutiny applied for the assessment
- Ensures that resources are focused on those IVDs associated with the greatest potential risk

GHTF Risk Classes and Risk Level

Classification	Personal Health Risk		Public Health Risk
Class A IVD	Low	and	Low
Class B IVD	Moderate	and	Low
Class C IVD	High	and/or	Moderate
Class D IVD	High	and	High

Application of Risk Classification Rules

- Varies depending upon setting in which a product is intended to be used
- Factors may differ between resource-limited settings compared to high-income countries
  - Endemicity and prevalence of infectious agents
  - Level of care available for a patient with the disease
  - Availability of follow-up or reference testing
  - Significant variations in training of professional users
- Therefore, risk classification of an IVD may be different depending where the product is used

Standards Organizations

- International Standards Organization (ISO)
  - QMS standard for manufacturing: ISO 13485:2003
    - Certification based on audits
    - Varying significance depending upon the quality and depth of the audit
  - Standards documents
- Clinical and Laboratory Standards Institute (CLSI)
  - Standards documents

Role of WHO

- Prequalification of diagnostics (PQDx)
- Regulatory capacity building

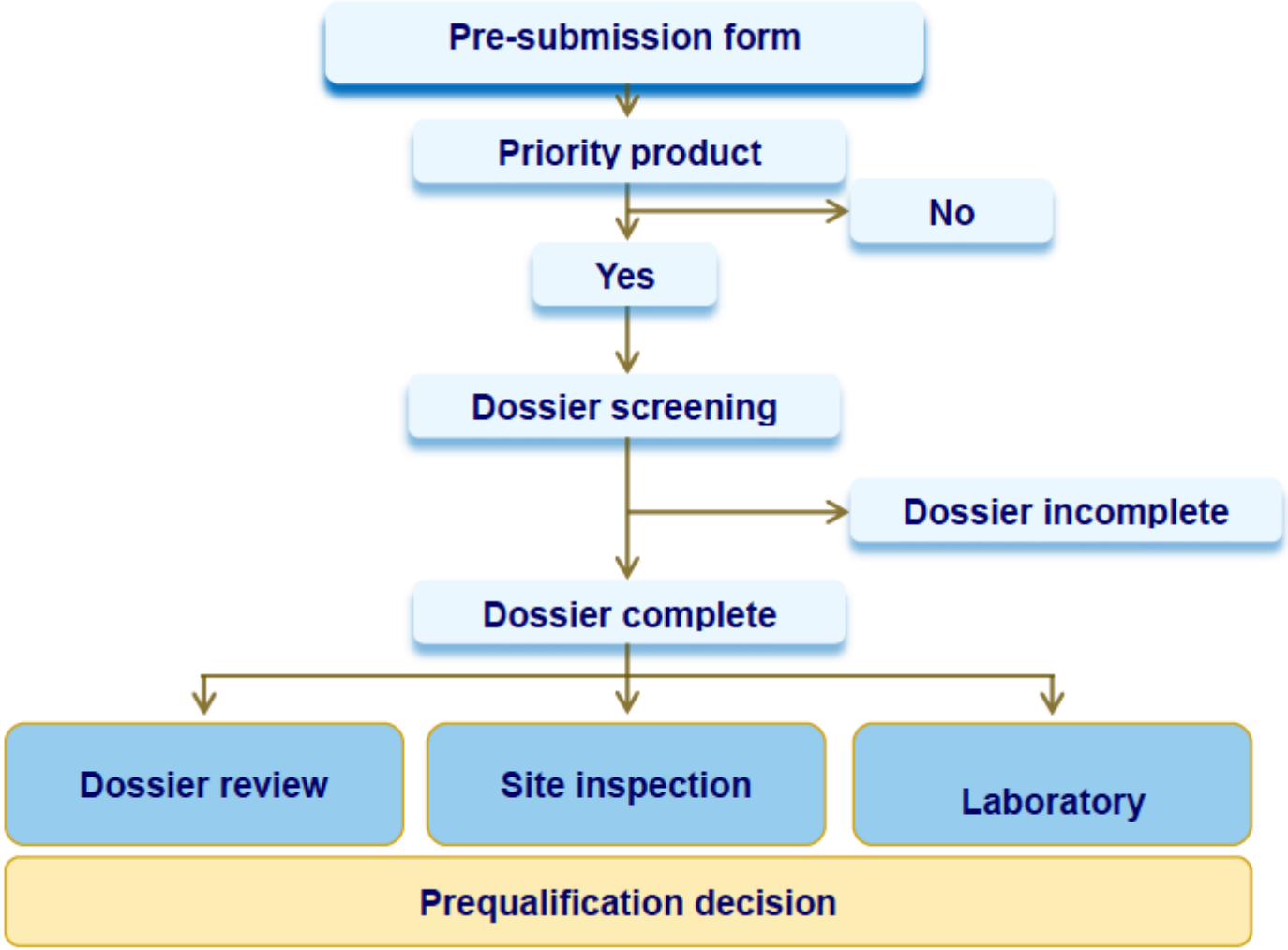
WHO Prequalification

- Designed to ensure that medicines, vaccines, diagnostics, and devices for high burden diseases meet global standards of quality, safety, and efficacy, in order to optimize the use of health resources and improve health outcomes
- Used by UN and other procurement agencies to make purchasing decisions regarding diagnostics, medicines and/or vaccines
- Does not imply WHO approval or endorsement

WHO Prequalification of Diagnostics (PQDx)

- Implemented in 2010
- Focus on the suitability of IVDs for use in resource-limited settings
- Accepts only a limited number of types of products for assessment, referred to as priority products
  - Decisions on priority-setting come from consultation with funding organizations and WHO disease programs
  - Designed to address the highest health priorities in resource-limited settings
  - Current PQDx priorities are HIV/AIDS, malaria and hepatitis B and C test kits and technologies

Overview of PQDx Process



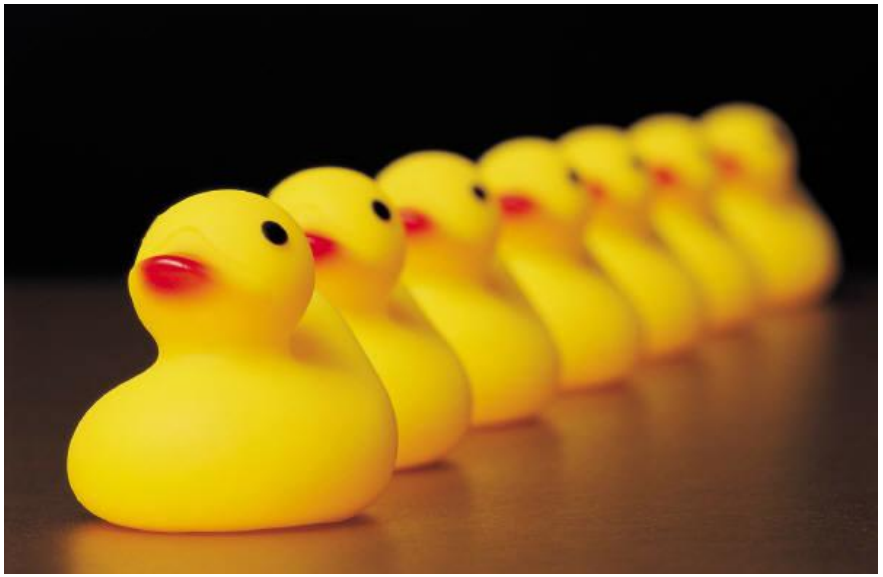
WHO: Regulatory Capacity Building

- Assisting Member States in developing robust systems for the regulation of medical products
- Primarily focused on medicines and vaccines (for now)

CONCLUDING THOUGHTS

HARMONIZATION VS. CONVERGENCE: ISSUES OF SENSITIVITY AND SPECIFICITY

Harmonization



- Doing it the same way
- One size fits all

Convergence

- Common goals
  - Quality-assured products
  - Conformance to global standards
- Not necessarily common methods
  - Respect for sovereignty
- Working together

Convergence – Another View

Gracias!