PQM Promoting the Quality of Medicines

Welcome

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Promoting the Quality of Medicines

Medicine Quality & Public Health Course at Boston University School of Public Health
Boston ◆ July 10-14, 2017

Medicines Regulation in Low and Middle Income Countries (LMICs)

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Promoting the Quality of Medicines Program
Global Public Health Programs | United States Pharmacopeial Convention

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COURSE SESSION OUTLINE

1. Medicines quality - why it is important?
2. Medicines regulation development and evolution
3. Medicines regulation implementing agencies, key regulatory functions and challenges
4. What factors contribute to effective medicines regulation?

COURSE SESSION OBJECTIVE

Provide participants some key information to increase understanding of Medicines Regulation and its evolution, and challenges in its implementation

MEDICINES QUALITY – ADAPTED WHO DEFINITION

The suitability of a medicinal product for its intended use is defined by:

- Its efficacy weighed against safety (health risks) according to a label claim or as promoted
- Its conformity to specifications regarding identity, strength, purity, and other characteristics, e.g., hardness, disintegration, dissolution property, impurity, sterility, etc.

- Medicine = API(s) + excipient(s) + information + package +labels

MEDICINES QUALITY – ADAPTED WHO DEFINITION

How can a medicine's quality be established, assessed/evaluated?

Medicines Situation in Most LMICs

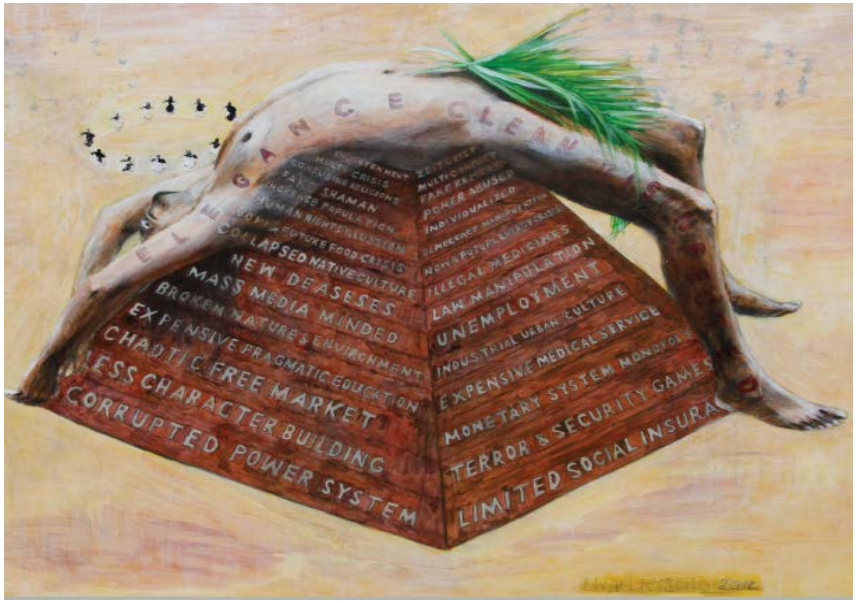
1. Most countries have an MRA and formal requirements for registering medicines, but differ substantially in their capacity and resources, and in their overall effectiveness.
2. The quality of medicines varies greatly in these countries in manufacturing and in the distribution system.
3. Regulatory gaps are common.
4. Three types of common imbalance have been identified in regulatory practice:
   - Over-concentration on pre-market post-market monitoring and regulating the distribution system
   - More attention given to inspection of manufacturing practice than of distribution channels.
5. Whilst regional and international harmonization of regulatory guidelines and practices are desirable, the current process allows inadequate expression of the needs.

MEDICINES REGULATION – BRIEF HISTORY

- BC 120 – Mithridates VI –Mithridatium contained 41 individual components for almost all diseases. In 1540 manufactured Mithridatium was subjected to supervision under Apothecaries Wares, Drugs and Stuffs Act
- 1581 1st Spanish Pharmacopoeia
- 1618 The London Pharmacopoeia
- After WWII modern medicines regulations started – knowledge base
- 1937 – DEG poisoning in USA – FDCA
- 1958-1960 – Thalidomide tragedy
- 1962 – the GMP compliance regulation

MAIN REASONS FOR REGULATING MEDICINES

The focus in Medicines Regulation and Public Health is on establishing and strengthening MRAs to develop norms and standards to ensure the quality, safety and efficacy of all pharmaceutical products and to put in place necessary infrastructures and procedures for QA/QC systems, as well make objective information available to the public



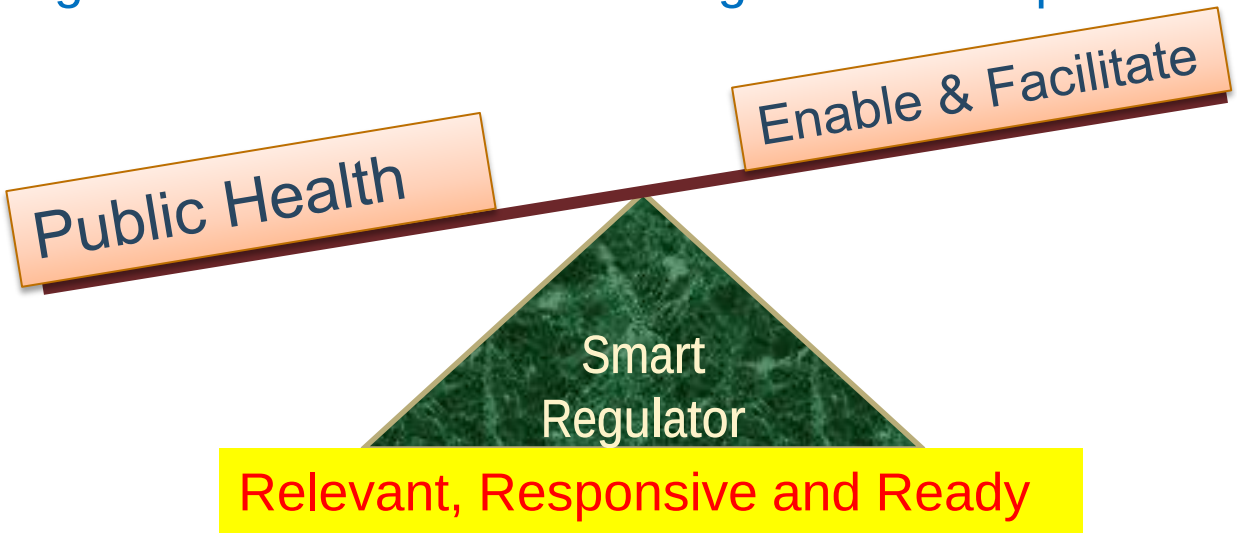
Main reasons for regulating medicines

1. **There is an 'information asymmetry' between those who manufacture/sell, prescribe/dispense medicines and patients/consumers, who are not equipped to make independent assessments of the quality, safety or efficacy of their medicines**
2. **In complex global pharmaceutical supply chains, there are many opportunities for unsafe products to be introduced before reaching the consumer**

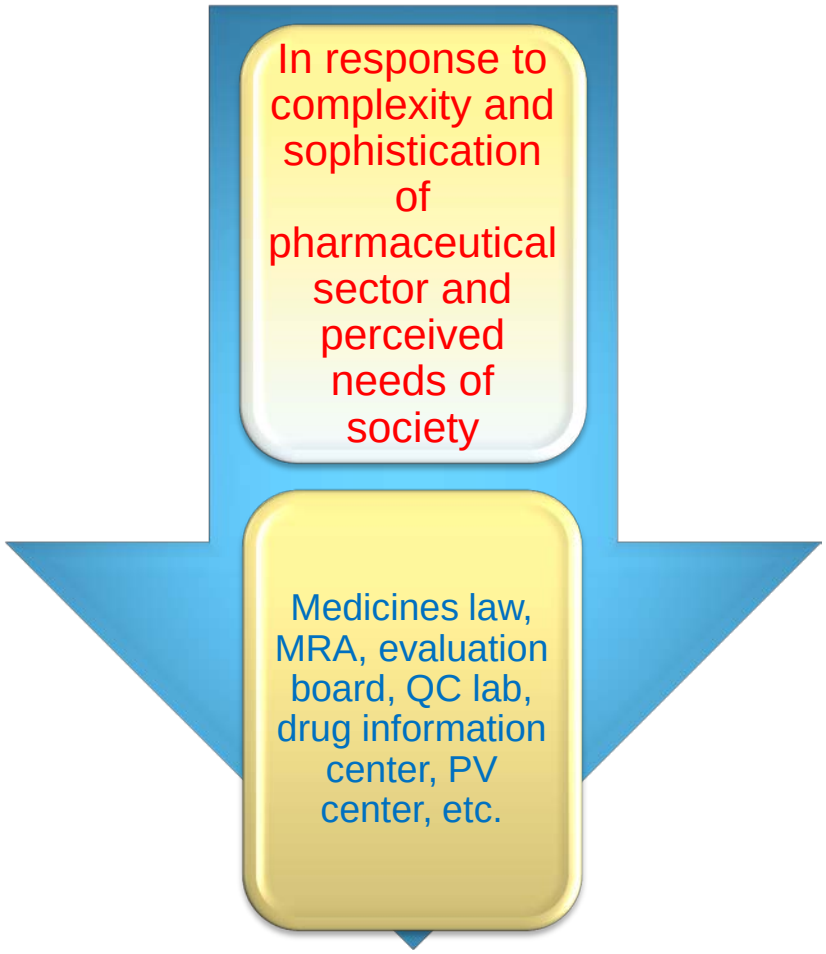
MEDICINES REGULATION – PURPOSE

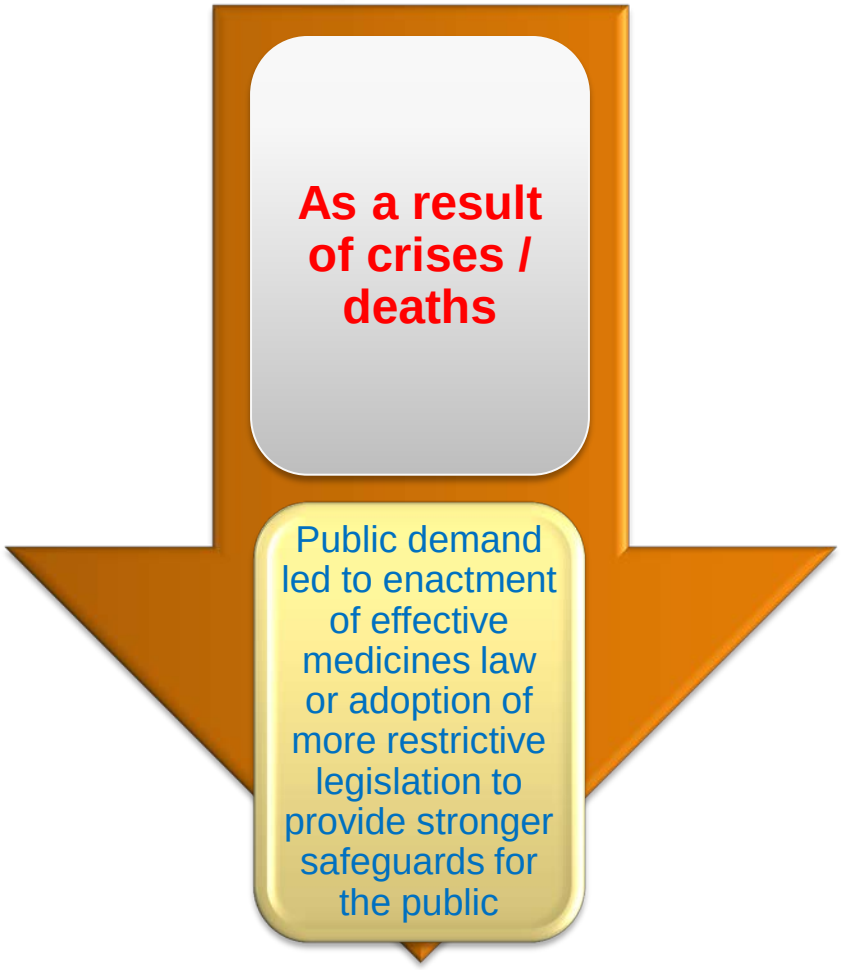
Medicines regulation incorporates several mutually reinforcing activities, all aim at promoting and protecting public health.

- Timely access to safe, efficacious and quality health products
- Good regulation can offer competitive economic advantage
- Supports development of dynamic, innovative and sustainable healthcare systems
- Being too cautious can cause negative consequences



DEVELOPMENT PATHS OF MEDICINES LAWS AND REGULATIONS





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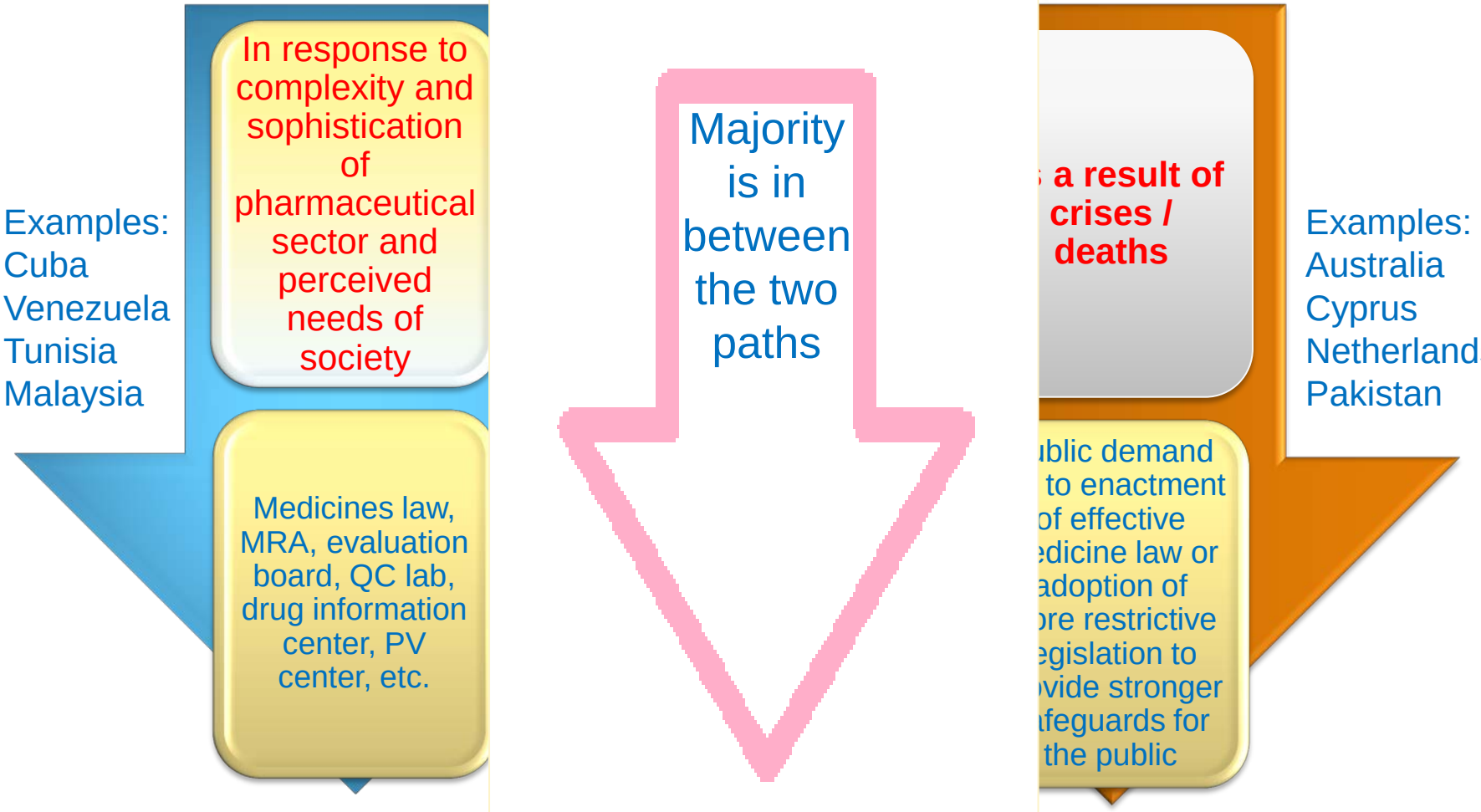

Consequently, ML&Rs need to be updated to keep pace with changes and new challenges in their environment

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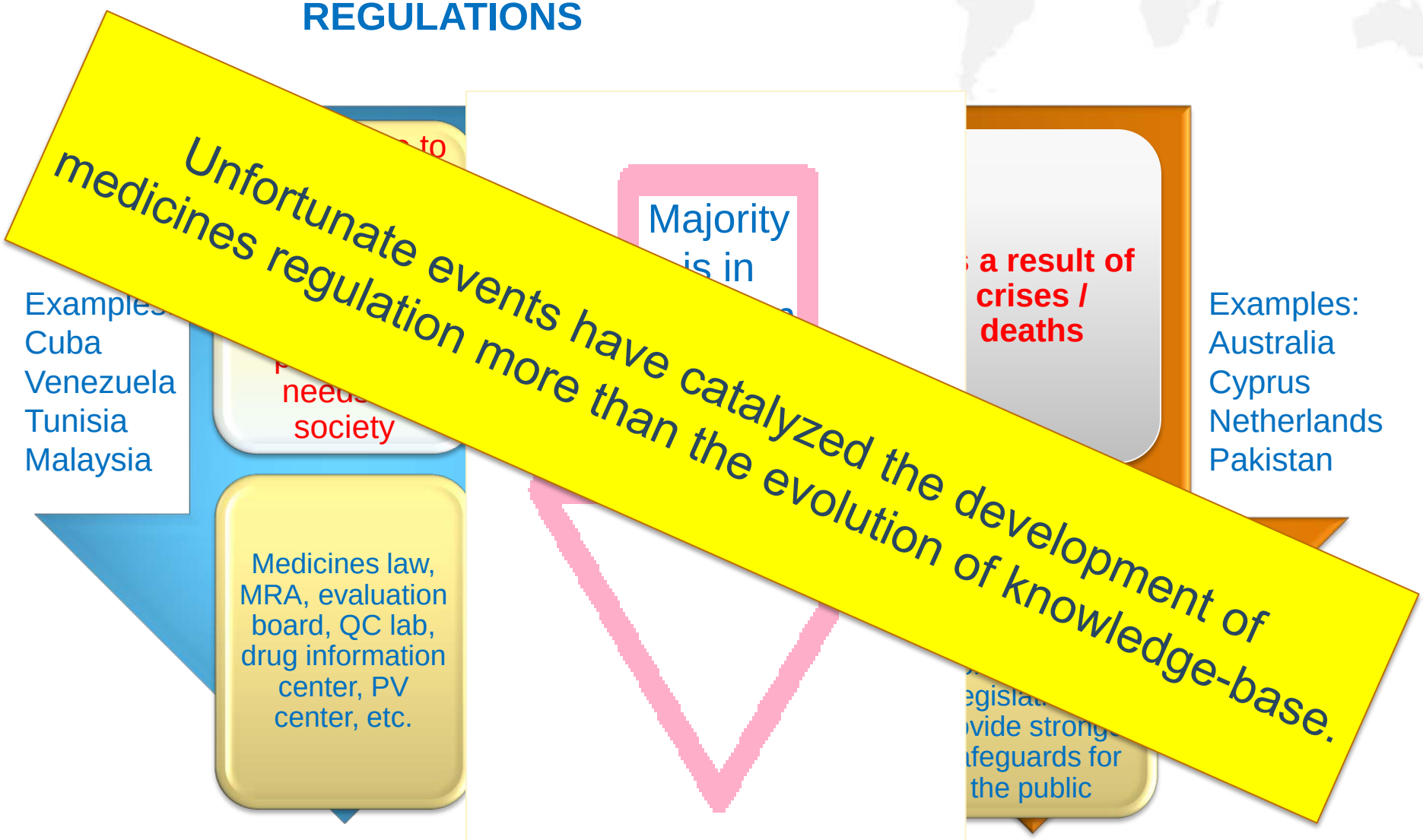

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THE EVOLUTION OF REGULATION: HISTORY OF THE U.S. FDA

1862 The newly formed Department of Agriculture analyzes food and other agricultural products under the Bureau of Chemistry, the early predecessor of today's FDA.

1883 Harvey Washington Wiley becomes Chief Chemist of the Bureau of Chemistry and expands the Bureau's food adulteration studies. He spends the next two decades as the "Crusading Chemist," reporting on food adulteration while campaigning for a federal law.

1906 Upton Sinclair publishes *The Jungle*, illustrating the horrors of the meat industry.

President Theodore Roosevelt signs the Pure Food and Drug Act and Meat Inspection Act into law. The laws ban food adulteration, deceptive labels, and the interstate sale of illegal food and drugs.

1927 The Food, Drug and Insecticide Administration is formed from the Bureau of Chemistry to house the food and drug regulatory and enforcement functions.

1931 The Food, Drug and Insecticide Administration is renamed the Food and Drug Administration.

1931

1937 1938 Elixir Sulfanilamide, a solution of the drug sulfanilamide (used to treat streptococcal infections) dissolved in poisonous diethylene glycol and sweetened with raspberry flavor, kills 107 people. There was no law requiring that new drugs be tested for safety.

In the wake of public outcry around the Elixir Sulfanilamide incident, the Federal Food, Drug, and Cosmetic Act becomes law. It requires manufacturers to prove safety before selling new drugs and brings medical devices and cosmetics under federal control.

1958 The Food Additives Amendment requires manufacturers of new food additives to prove safety.

1962 A antiemetic that the FDA blocked from entering the United States is identified as the cause of thousands of birth defects in Europe. Public support for tougher drug regulation increases.

1976 The Medical Device Amendments classify medical devices in three categories based on risk levels and regulate them accordingly. The amendments are passed after thousands of women are injured by the Dalkon Shield intrauterine device.

2011 The Food Safety Modernization Act expands the FDA's powers with the goal of building a food safety system based on prevention.

REGULATORY FRAMEWORK

ADMINSTRATIVE ELEMENTS:

- ☐ Policy, legislation and regulations
- ☐ Human resources
- ☐ Finance
- ☐ Infrastructure

TECHNICAL ELEMENTS:

- Standards
- Specs
- Guidelines
- Procedures

REGULATORY FUNCTIONS

- Product assessment and registration/ marketing authorization
- Licensing of premises, practices and persons
- Inspection of manufacturers, distributors, and retailers
- Quality and ADR monitoring and PMS
- Control of promotion and advertising
- Laboratory Access and Testing
- NRA Lot release of Vaccines
- Control of imports and exports of medicines
- Clinical Oversight

REGULATION LEVEL:

- Central
- State or provincial
- District
- community

NON REGULATORY FUNCTIONS

- Manufacturing
- Procurement and supply
- Price control*

Source: Adapted from Ratanawijitrasin and Wondemagegnehu. 2002. Effective Drug Regulation: A Multicountry Study. WHO 2002.

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Central coordination and information sharing – under IRIMS

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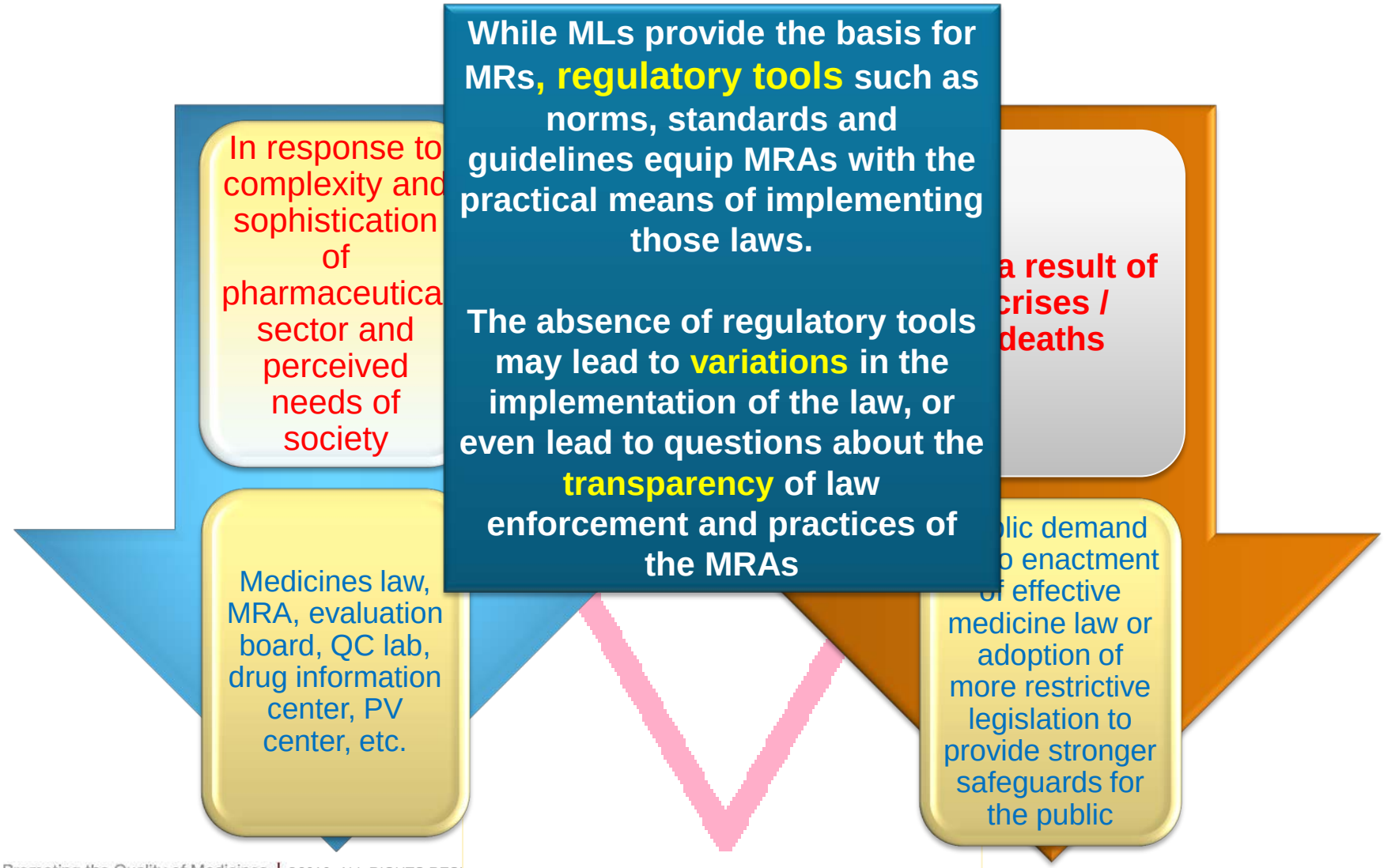
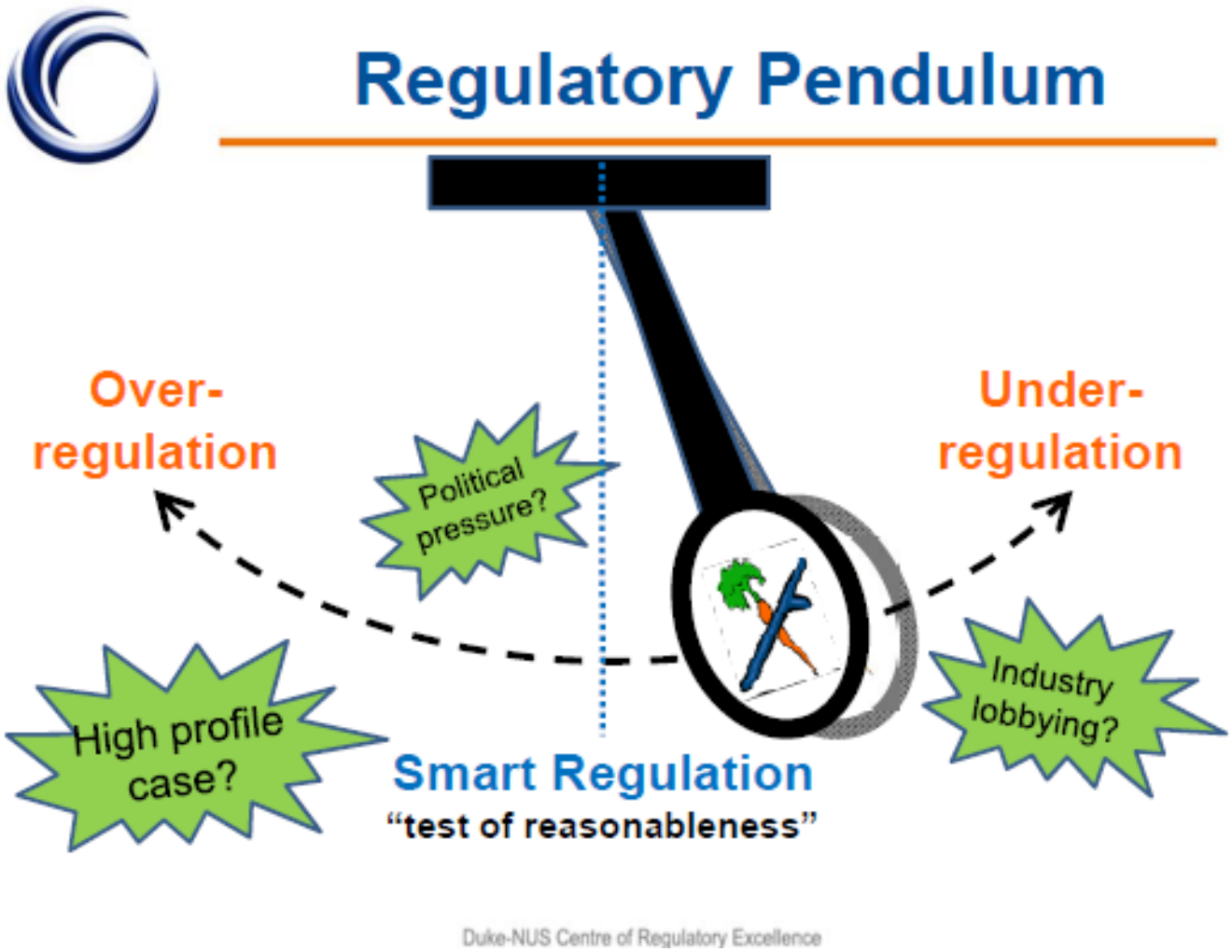


Evolving regulatory approaches



Source: John Lim, 2016. Overview of Centre of Regulatory Excellence. Presentation presented at United States Pharmacopeial Convention.

Increase Relevance in Regulation

1. Continuing systematic review of existing rules and regulations to ensure relevance and effectiveness
   - ❖ Quality management systems
   - ❖ Regulatory impact analyses

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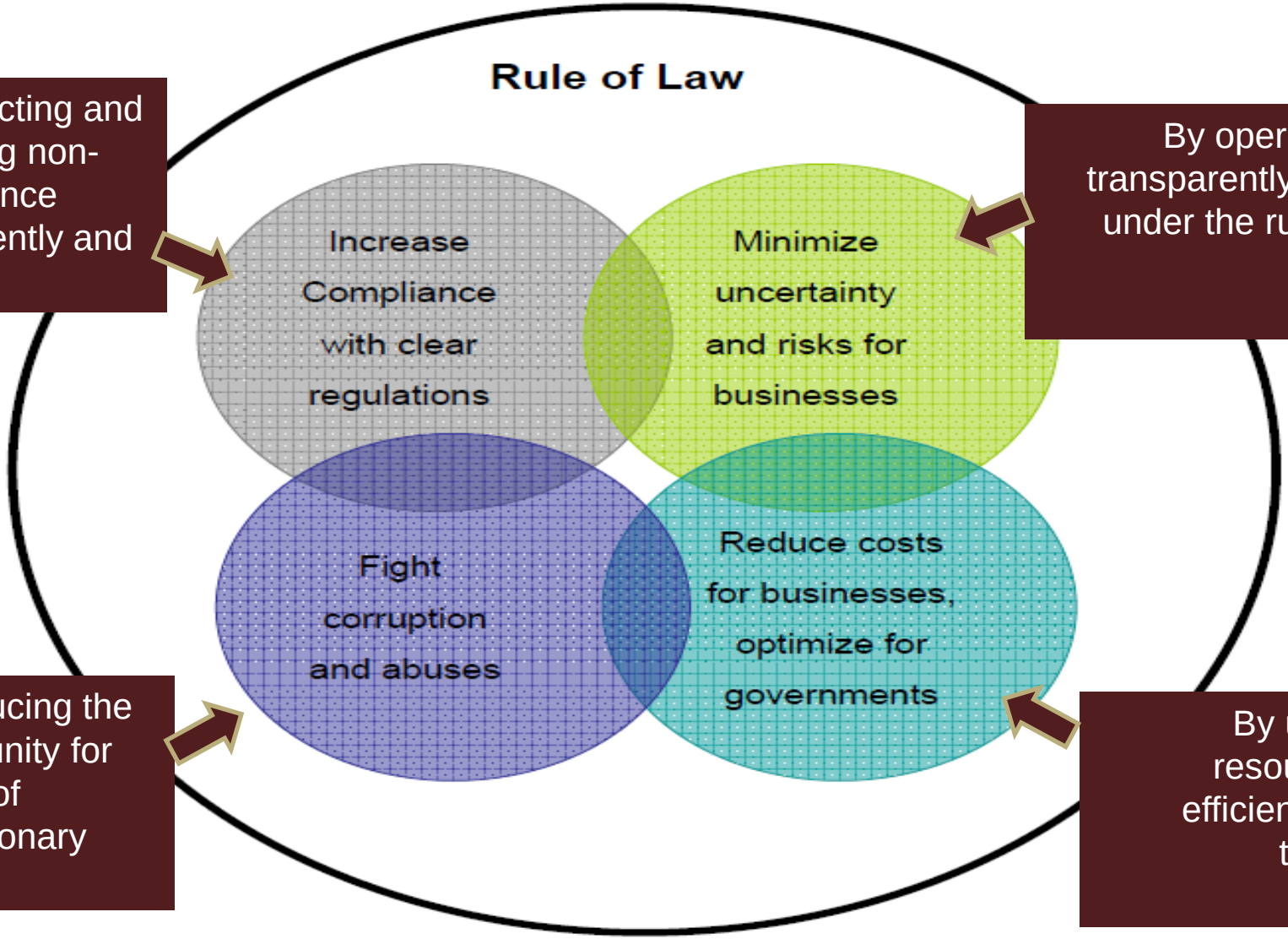
1. **Ensuring well-informed stakeholder population**
   - ❖ Effective communication and engagement of stakeholders

MEDICINES REGULATION – PROTECTING PUBLIC

By detecting and deterring non-compliance consistently and fairly

By operating transparently and under the rule of law



By reducing the opportunity for abuse of discretionary powers

By using resources efficiently to target

Source: The World Bank, 2005. Good Practices for Regulatory Inspections: Guidelines for Reformers

MEDICINES REGULATION – THE UNKNOWNS

Areas where regulators do not have:

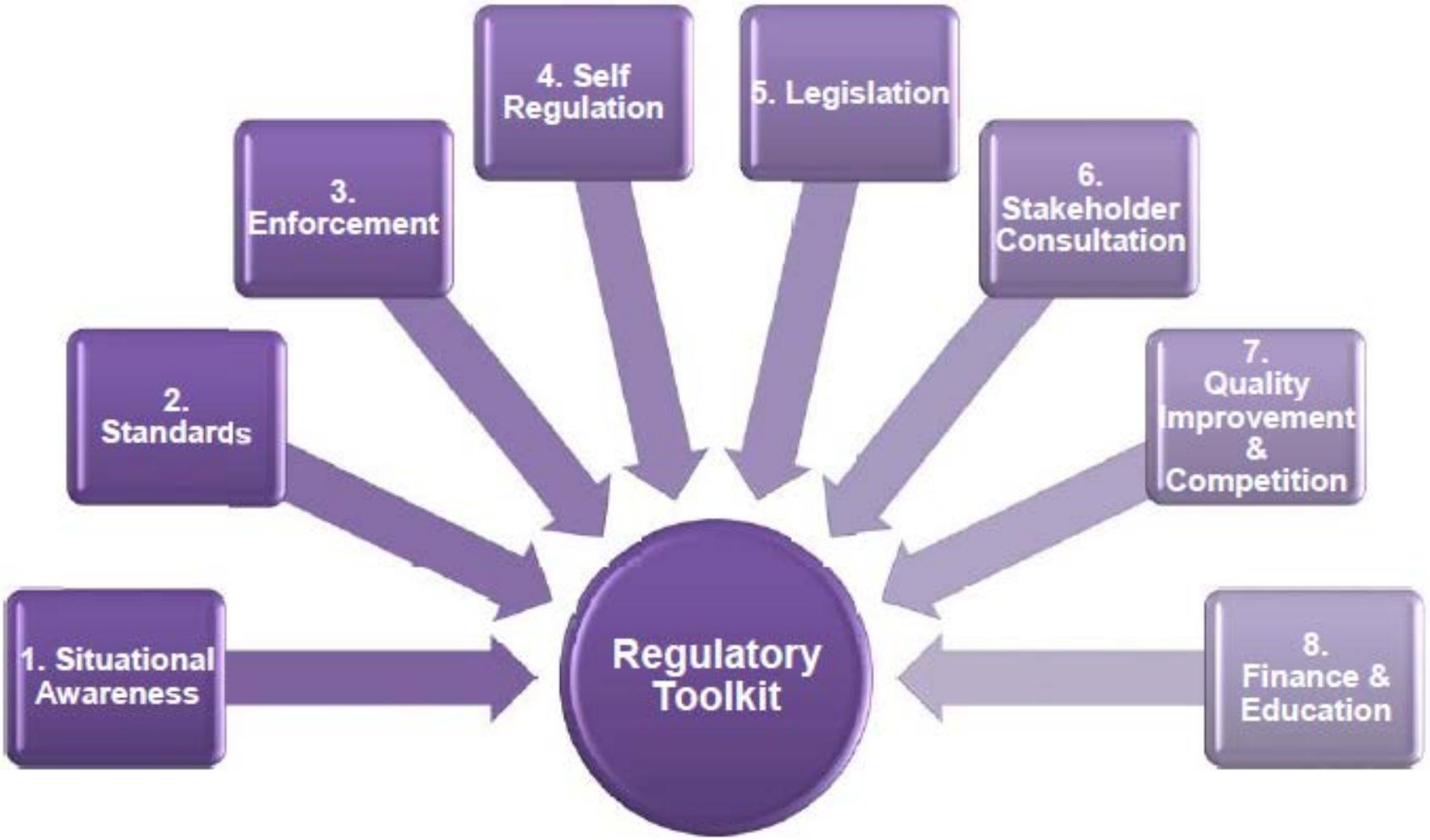
- Expertise and skills
- Adequate data
- Intention to regulate directly due to, in part, above
- Clear regulatory mandate
- Adequate law and regulations to back them up

Regulators would then face challenges in defining regulatory space and balance:

- What are regulators' obligations and at what level to regulate?
- What are stakeholders' expectations?
- How to communicate to align obligation with expectations?

At any rate, public may still hold regulator responsible and accountable for if severe adverse reactions or events occur.

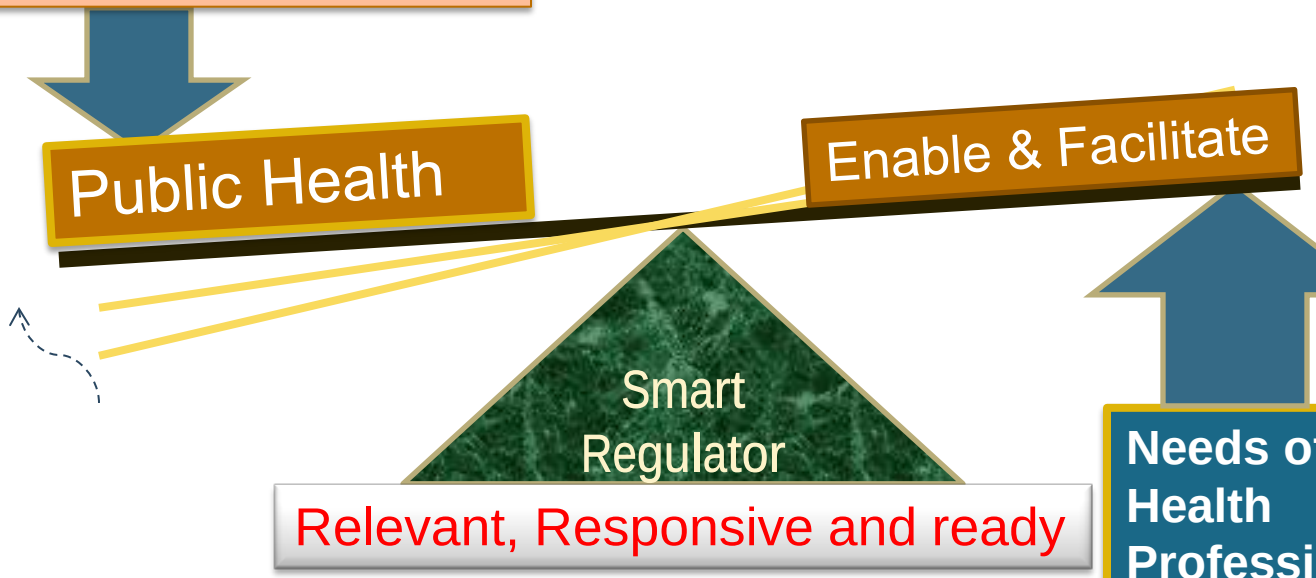
MEDICINES REGULATORY TOOLKIT



REGULATORY BALANCE

Protect public health and safety

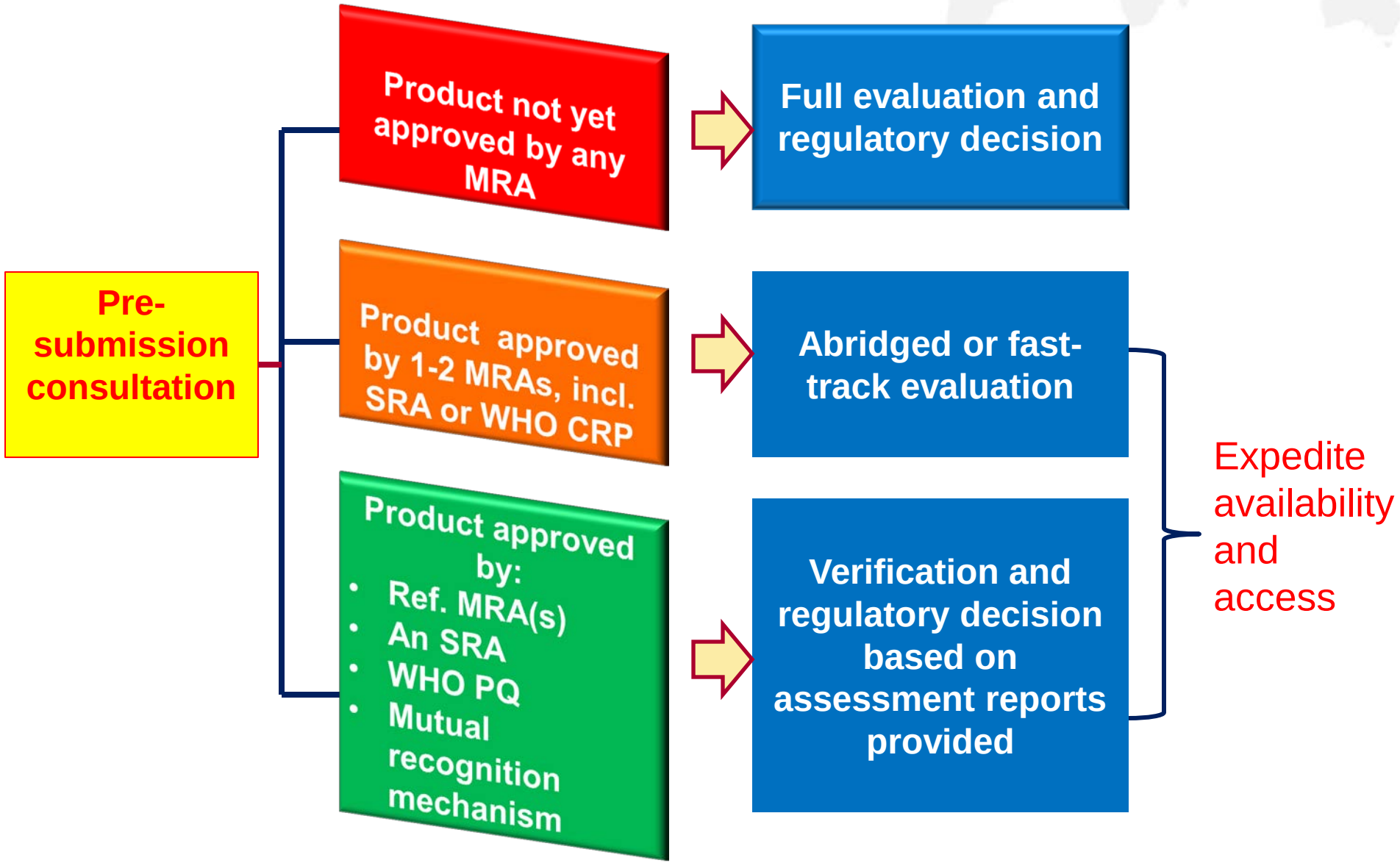
- Allow timely access to QSE as well as innovative therapies and products



Needs of Public, Health Professionals and Industry

- Be sensitive to concerns
- Apply user-friendly policies

ADOPTING RISK-BASED REGULATION

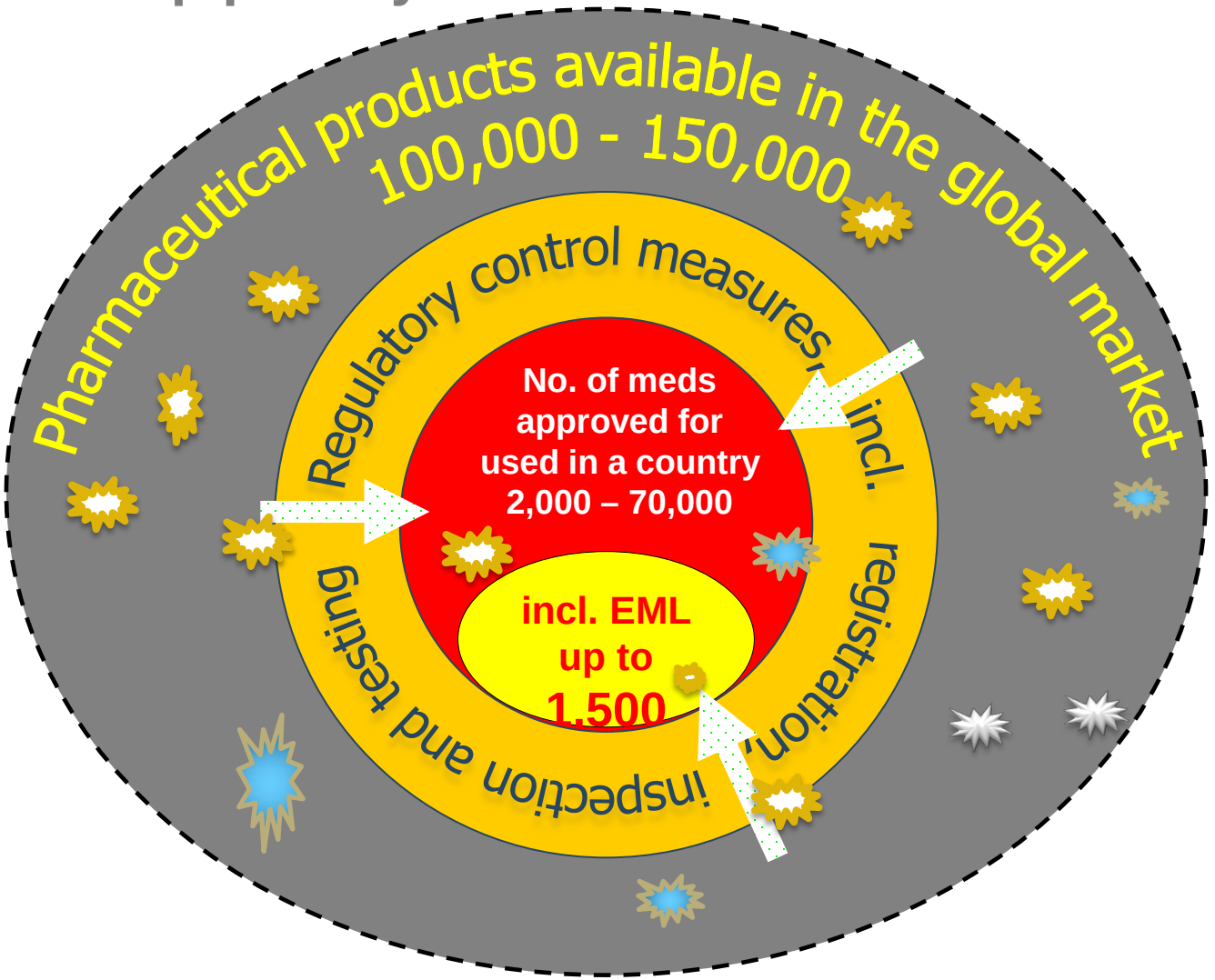


TREND TOWARDS HARMONIZATION

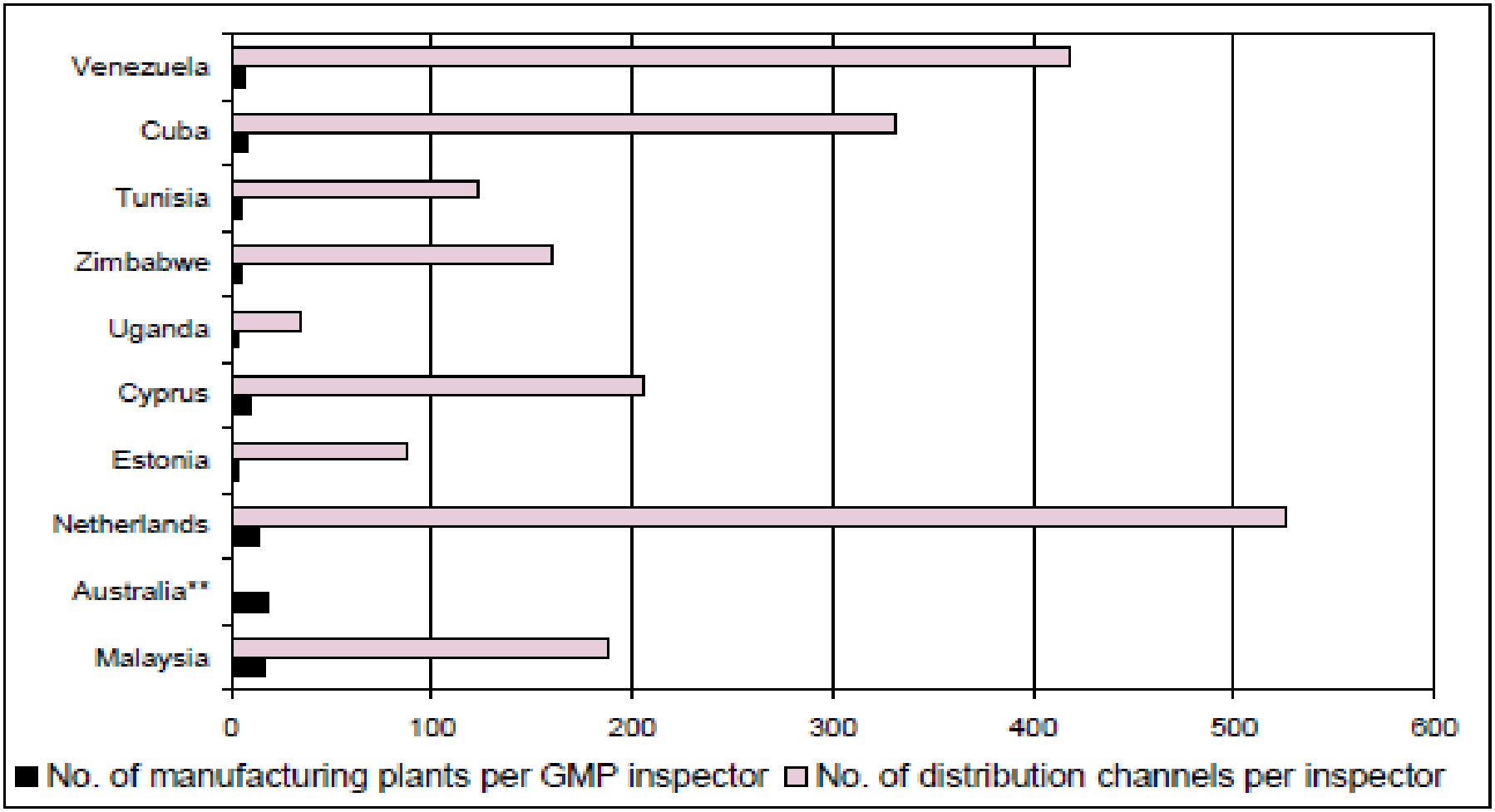
Regional and international collaboration in drug regulation has led to the creation of regional and international instruments to facilitate control and harmonization of technical and regulatory requirements. Examples are:

1. European Medicines Evaluation Agency (EMEA)
2. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) to achieve greater harmonization to ensure that safe, effective, and high quality medicines
3. The Association of South-East Asian Nations (ASEAN) on application for registration (ACTD), GMP inspection, and BA/BE protocol
4. PIC/S on GMP inspectorate standards
5. International Conference of Drug Regulatory Authorities (ICDRA)
6. New Partnership for Africa's Development (NEPAD) thru East African Community Medicines Regulatory Harmonization (EAC/MRH) program, African Drug Regulatory Authority Network (AFDRAN)

Challenges in regulatory measures for quality assured medicines: registration, licensing & inspection, and testing – what should be the top priority?



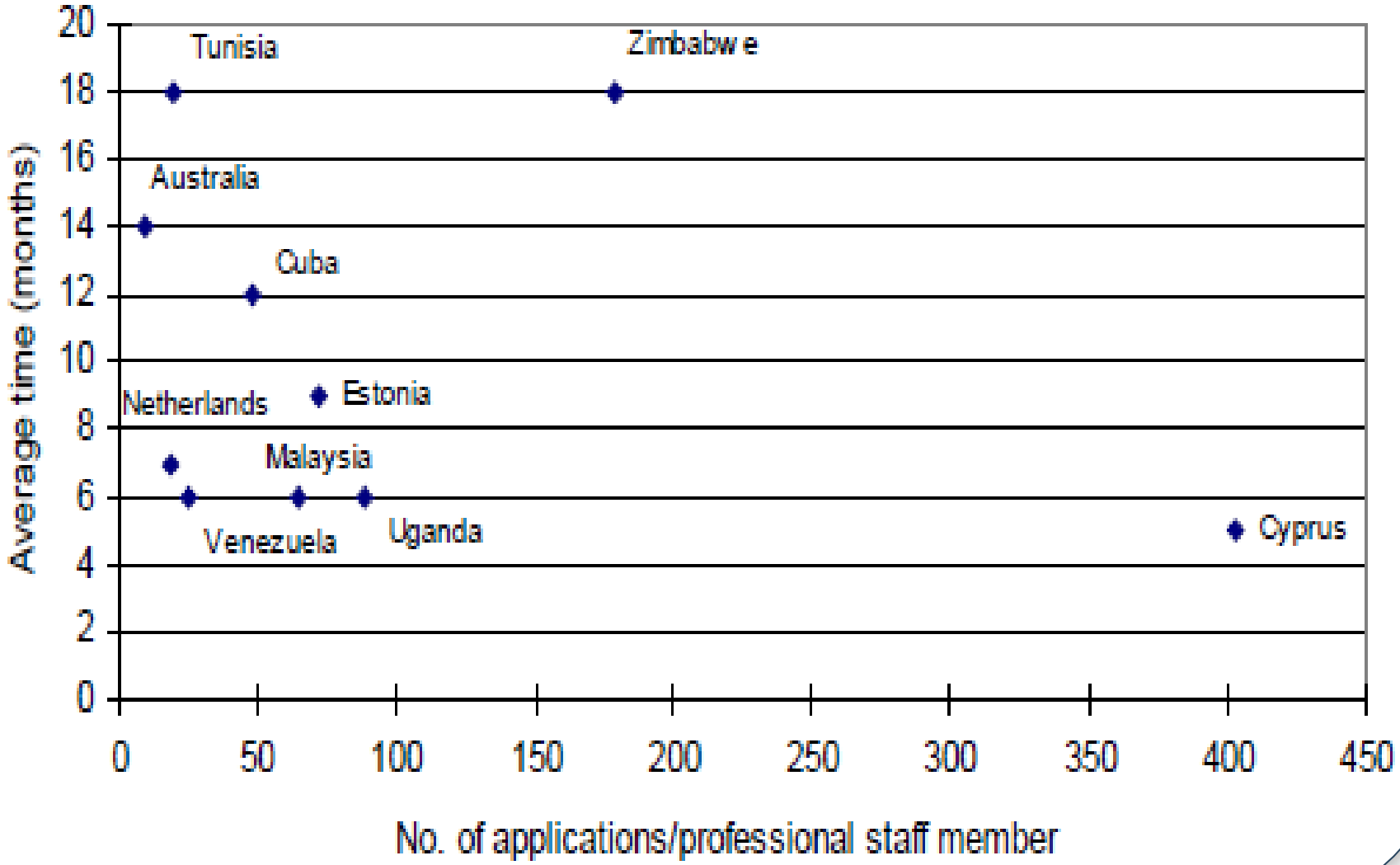
Challenges in key regulation areas: workload of inspectors



* *Distribution channels — includes all types of drug outlet.*

** *For Australia, no data are available about the number of distribution-channel inspectors.*

Challenges in key regulation areas: workload of product evaluators



What factors contributing to effective regulation within an MRA?

Exercise – 5 minutes

Based on your experience, please name 4-5 factors that contribute to the effectiveness of medicines regulation (in your country):

1. …
2. …
3. …
4. …
5. …

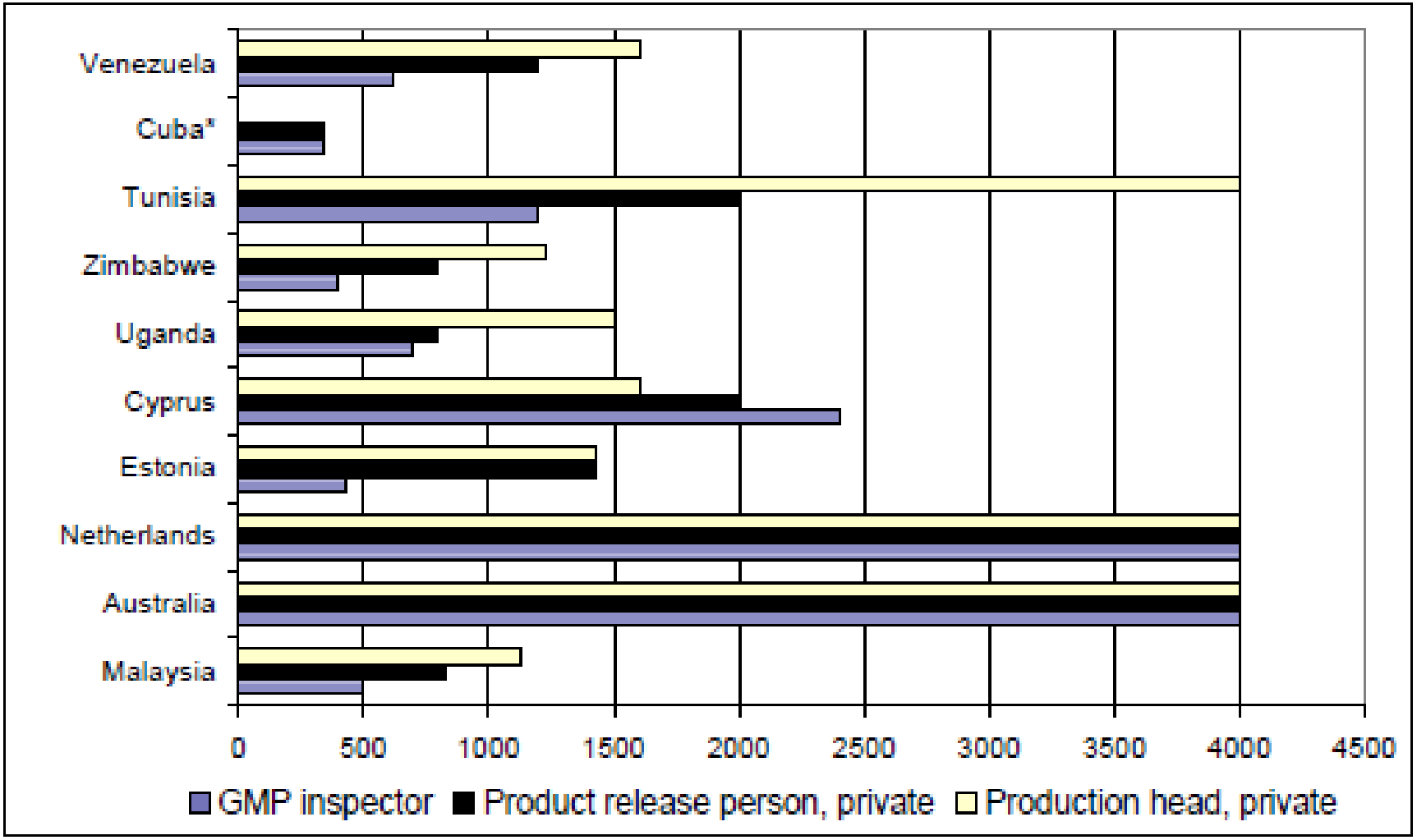
WHAT FACTORS CONTRIBUTING TO EFFECTIVE MEDICINES REGULATION IN GENERAL CONTEXT?

1. **Political will** and commitment to regulation
2. Adequate supply of medicines at affordable prices
3. Strong public support for drug regulation and regulatory system
4. Effective cooperation between the national medicines regulatory authority (MRA) and other government law enforcement agencies (e.g. customs and police)
5. Sufficient qualified and experienced pharmaceutical and other health professionals
6. Political environment favoring independent technical decision-making
7. Effective legislation to support and empower MRA to carry out its key functions and responsibilities

What factors contributing to effective regulation within an MRA?

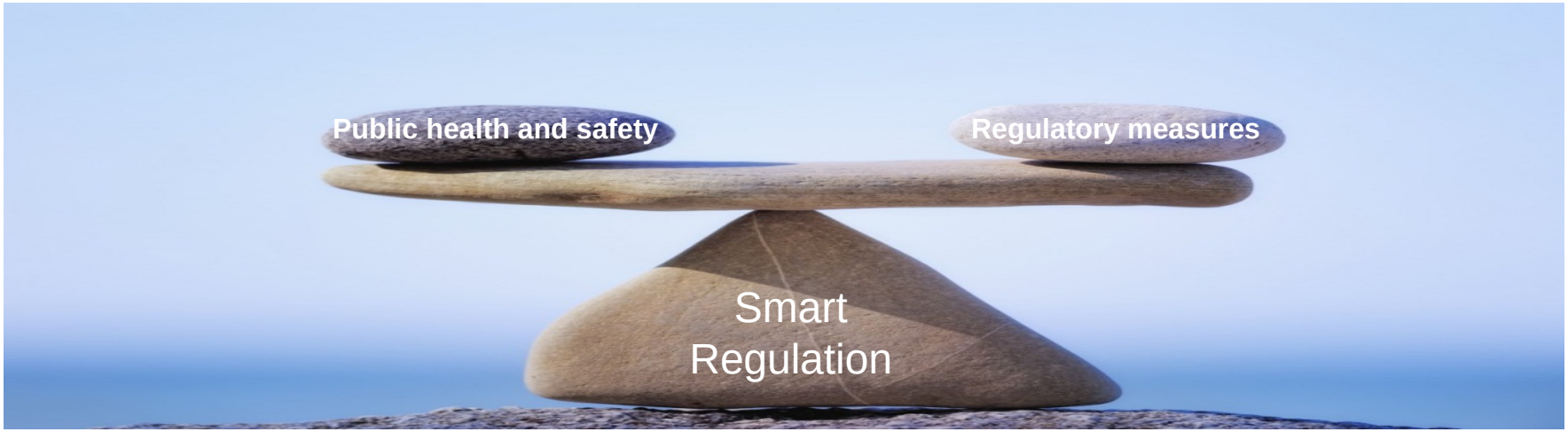
1. Clear mission
2. Adequate medicines legislation and regulation
3. Appropriate organizational structure and facilities
4. Clearly defined roles and responsibilities
5. Adequate and sustainable financial resources, including resources to retain and develop staff
6. Appropriate tools, such as standards, guidelines and procedures
7. Strong cooperation and collaboration between MRAs and other stakeholders
8. Accountability and transparency
9. Good management system

Would financial imbalance between regulator and his/her private counterpart affect the effectiveness of medicines regulation?



CONCLUSION

If a medicines regulation is to bring about the ultimate outcome of protecting public health and safety with quality assured, safe, and efficacious medications, certain structural , process arrangements must be securely in place.



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- The Boston University School of Public Health
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Promoting the Quality of Medicines

Thank You

Inquiries? Please contact:
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