World Health Organization

WHO Good Regulatory Practices and Good Reliance Practices

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Inter-American Coalition for Regulatory Convergence Virtual Meeting

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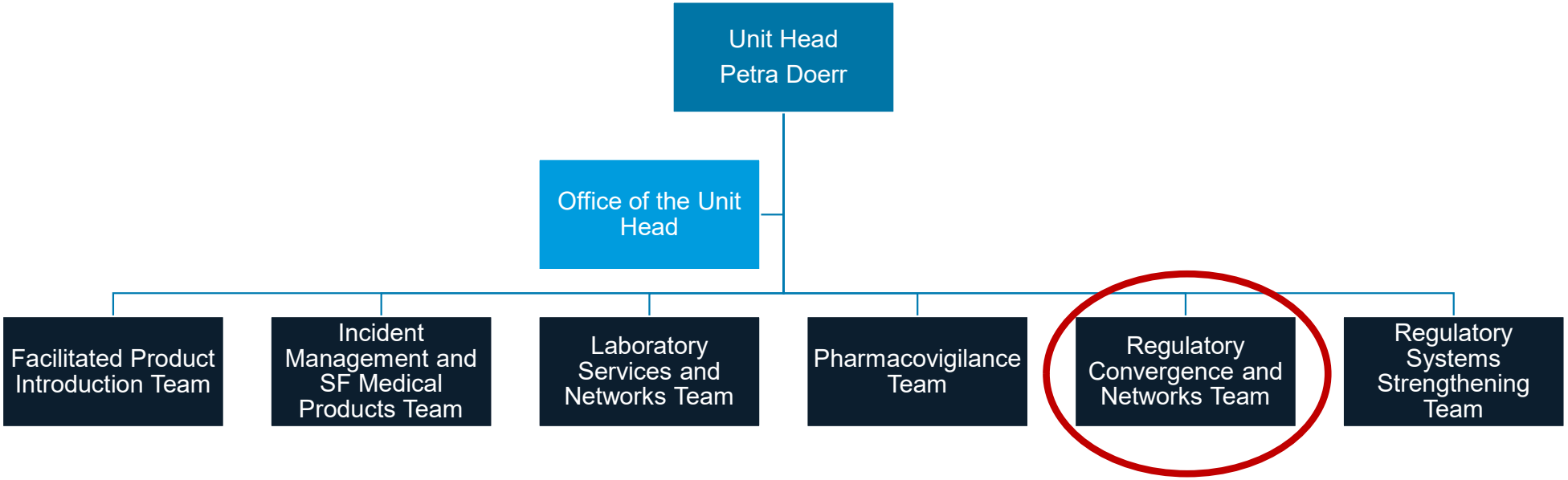
World Health Organization

"Quality medical products are essential to human health, and a vital part of every health system."

Dr Tedros Adhanom Ghebreyesus
WHO Director General

Regulation and Safety (REG) Unit within the Regulation and Prequalification Department



Outline

World Health Organization

- WHO Regulatory System Strengthening activities
- Good Regulatory Practices Principles
- Good Reliance Practices Principles

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World Health Organization

WHO Regulatory System Strengthening activities

Good Regulatory Practices Principles

Good Reliance Practices Principles

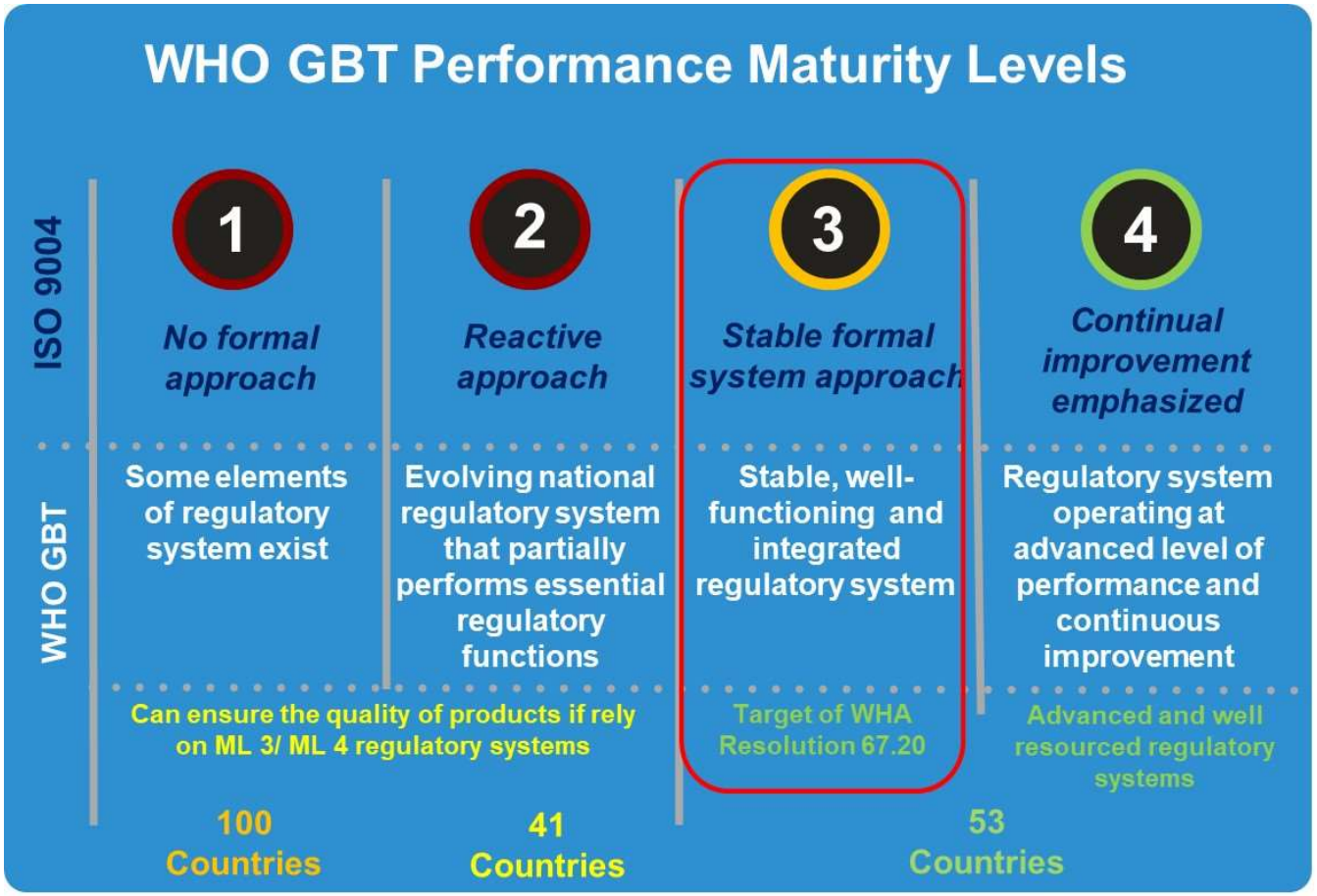
Objectives of the WHO regulatory system strengthening programme

1. • **Build regulatory capacity** in Member States consistent with good regulatory practices

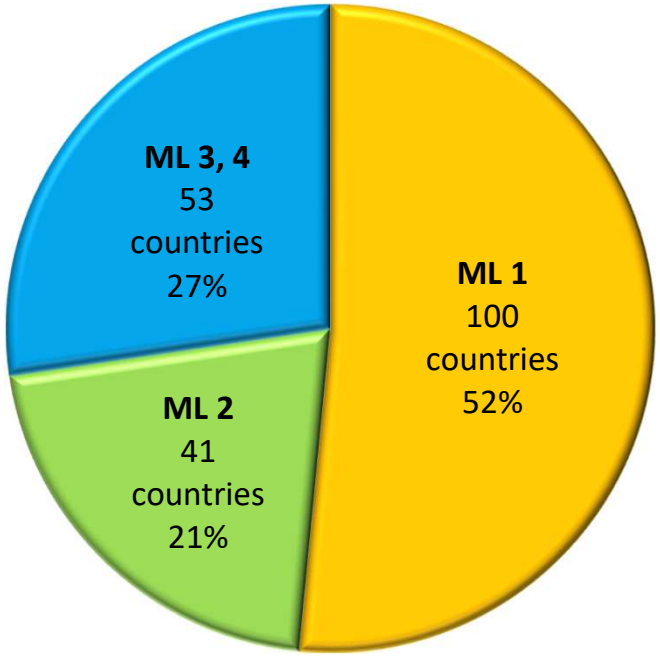
2. • **Promote regulatory cooperation, convergence and transparency** through networking, work-sharing and reliance

- **World Health Assembly Resolution 67.20 in 2014**
  - ✓ recognized the importance of strong regulatory systems to a well-functioning healthcare system and the attainment of health-related United Nations Sustainable Development Goals and Universal Health Coverage.

WHO Benchmarking of National Regulatory Authorities (NRAs)



Overall regulatory systems' maturity level of WHO Member States and major challenges



2020

Main challenges:

- Lack of national policy and long-term strategy
- Unclear vision and mission (what should be done and what should not)
- Insufficient commitment and engagement from political level (access and price vs. quality)
- Inadequate resources to establish and sustain regulatory oversight
- "Bad Regulatory Practices"

Countries Institutional Development Plans

Outline

World Health Organization

- WHO Regulatory System Strengthening activities
- **Good Regulatory Practices Principles**
- Good Reliance Practices Principles

WHO Good Regulatory Practices

Response to requests for **guidance in addressing common gaps in regulatory practices** identified during benchmarking exercises

Set of principles and practices applied to the development, implementation and review of regulatory instruments in order to achieve a public health policy objectives in the most efficient way

Relevant to all regulators, irrespective of resources, maturity or regulatory models (national, supranational and multiple institutions)

WHO Good Regulatory Practices

World Health Organization

Purpose

- Present the **high-level principles** of Good Regulatory Practices.
- Principles to serve as **benchmarks**.
- Guide Member States in **prioritizing** their regulatory activities according to; resources, national goals, public health policies, medical products policies and the medical product environment

Scope

- **Relevant to all regulators**, irrespective of resources, maturity or regulatory models; equally applicable to supranational (e.g. regional), national and subnational regulatory systems.
- **Related audience**: institutions and policy-makers, regulatory networks, regulated parties

WHO Good regulatory practices in the regulation of medical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations: Fifty-fifth report. Technical Report Series, No. 1033, Annex 11; 2021. Link: https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations

WHO Good Regulatory Practices

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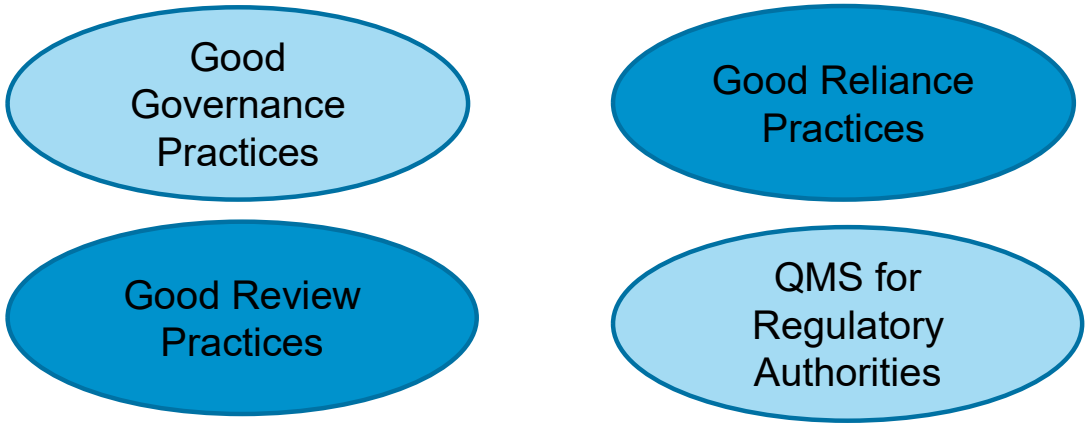
Objectives:

- Ensure sound and effective regulation of medical products.
- Higher-quality regulation, better regulatory decision-making and compliance.
- More efficient regulatory systems and better public health outcomes.
- Up to date regulatory systems.
- Promote trust among regulatory authorities and other stakeholders.
- Facilitate international cooperation.

Complemented by:



Nine high-level principles

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Legality	Consistency	Independence
Impartiality	Proportionality	Flexibility
Clarity	Efficiency	Transparency

GRP main principles

1. Legality

All GRP Principles linked to GBT EXAMPLE

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Regulatory systems and the decisions that flow from them must have a sound legal basis

Key elements:

- Authority, scope and flexibility to safeguard and promote health
- Delegation of power and responsibilities
- Support and empower international cooperation
- Possibility to review regulatory decisions and sanctions
- Scope and lines of authority of involved institutions
- Accountable

GBT:

MA01.01: There are legal provisions that require the receipt of a registration or marketing authorization (MA) before placing the product on the market.

MA02.01: There is a defined structure with clear responsibilities to conduct registration or MA activities

RS09.01: The NRA participates in regional and/or global networks to promote convergence and harmonization efforts and expand its collaboration in the regulatory field.

RS01.09: A guideline on complaints and appeals against regulatory decisions is available to the public.

Enablers for Good Regulatory Practices (1/2)

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1. **Political and government-wide support**: Sustained support at the highest political and government levels, including policy makers, is essential for the proper implementation of the concept and principles of GRP.

2. **Effective organization and good governance supported with leadership:** Leadership is critical for setting and carrying out the organizational vision, mission, policies and strategies which in turn significantly contribute to organizational efficiency.

3. **Inter-and-intra-organizational communication, collaboration and coordination:** Adequate and effective communication plays a fundamental role for exchanging information within and outside the institutions forming the regulatory system. When regularly communicating both internally and externally, regulatory authorities remain more transparent and accountable.

4. **A robust and well-functioning quality management system**: which includes the application of quality risk management (QRM) principles, is a valuable tool that helps regulatory authorities to achieve greater credibility for their decisions, and greater stability and consistency in their operations

Enablers for Good Regulatory Practices (2/2)

World Health Organization

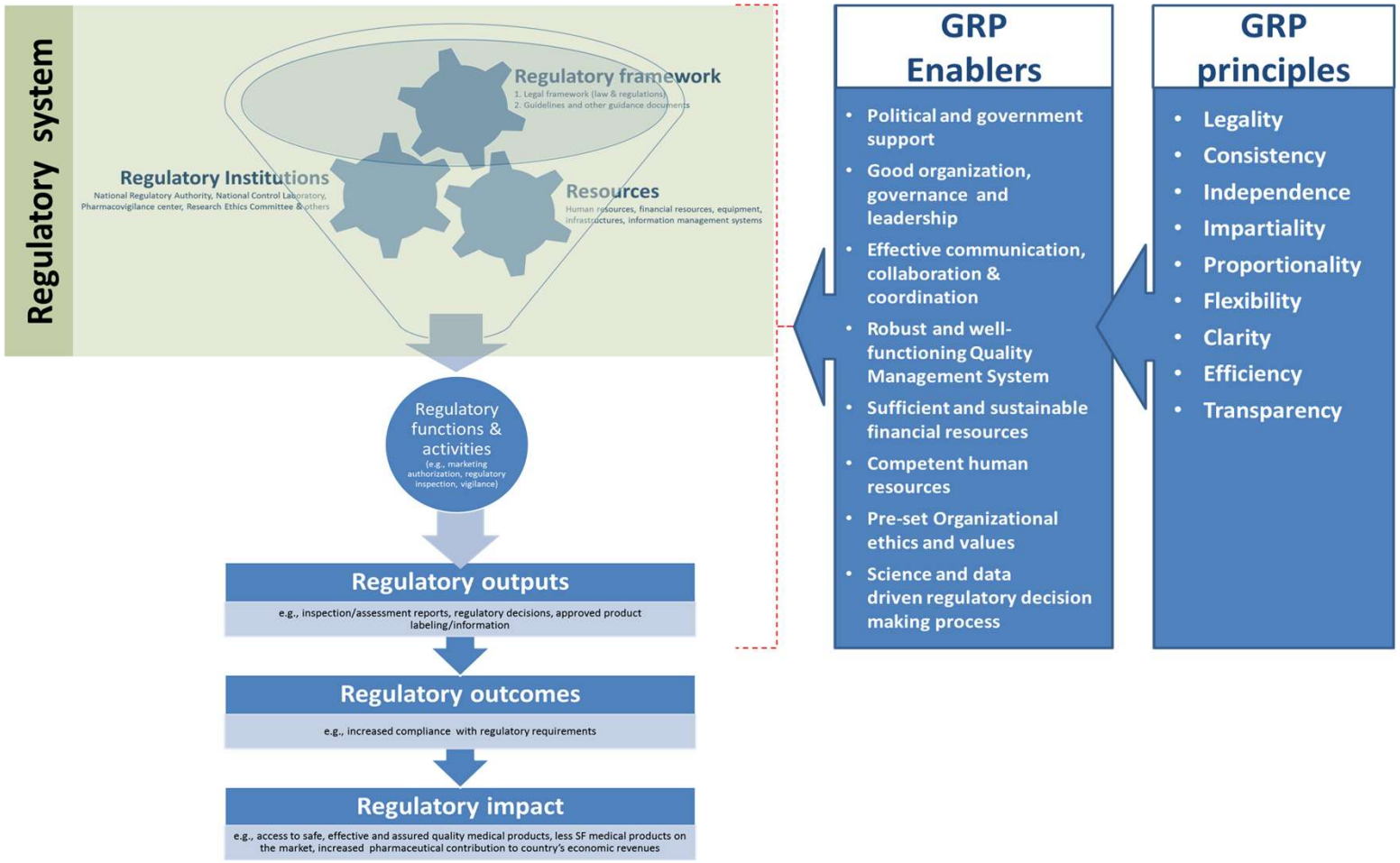
5. Sufficient and sustainable financial resources: Investment in regulatory systems is critical to a well-functioning health care system. Securing financial resources to effectively carry out the regulatory mandate and to continuously improve the performance of regulatory activities is an essential enabler for regulatory system independence, impartiality, consistency and efficiency.

6. Competent human resources: An array of technical and scientific knowledge and the skills of regulatory staff contribute to the development, implementation and maintenance of a regulatory system for medical products. Personal and career development policies and measures are critical for regulatory authorities to attract and recruit competent staff and, in addition, to retain competent staff in the service.

7. Pre-set organizational ethics and values: Regulatory personnel should abide by ethical principles, organizational values, and professionalism (e.g. Code of conduct).

8. Science- and data-driven decision-making process: Regulatory decisions, along with their making process, should be based on scientific foundations and accurate data rather than intuitions or arbitrariness. Adherence to international standards and guidelines represent key enablers to science-based regulatory decision-making.

Good Regulatory Practices Summary



Principles and enablers of Good Regulatory Practices (GRP) and Components of the regulatory system

Good Regulatory Practices

Any questions?

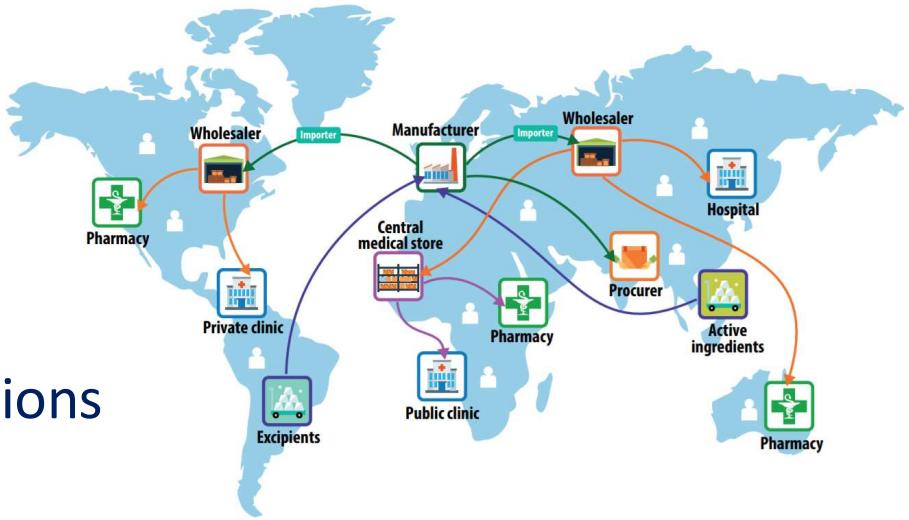
Outline

World Health Organization

- WHO Regulatory System Strengthening activities
- Good Regulatory Practices Principles
- **Good Reliance Practices Principles**

Evolving Science and Regulatory Challenges

- Globalization of markets
- Sophistication of health technologies
- Rapid evolution of regulatory science
- Increasing complexity of supply chains
- Transparency and growing public expectations
- Lack of global regulatory resources



Importance of international cooperation to **ensure the safety, quality and efficacy/performance** of locally used medical products

Make best use of available resources and expertise, avoid duplication and **concentrate regulatory efforts and resources** where most needed

Principles of Reliance

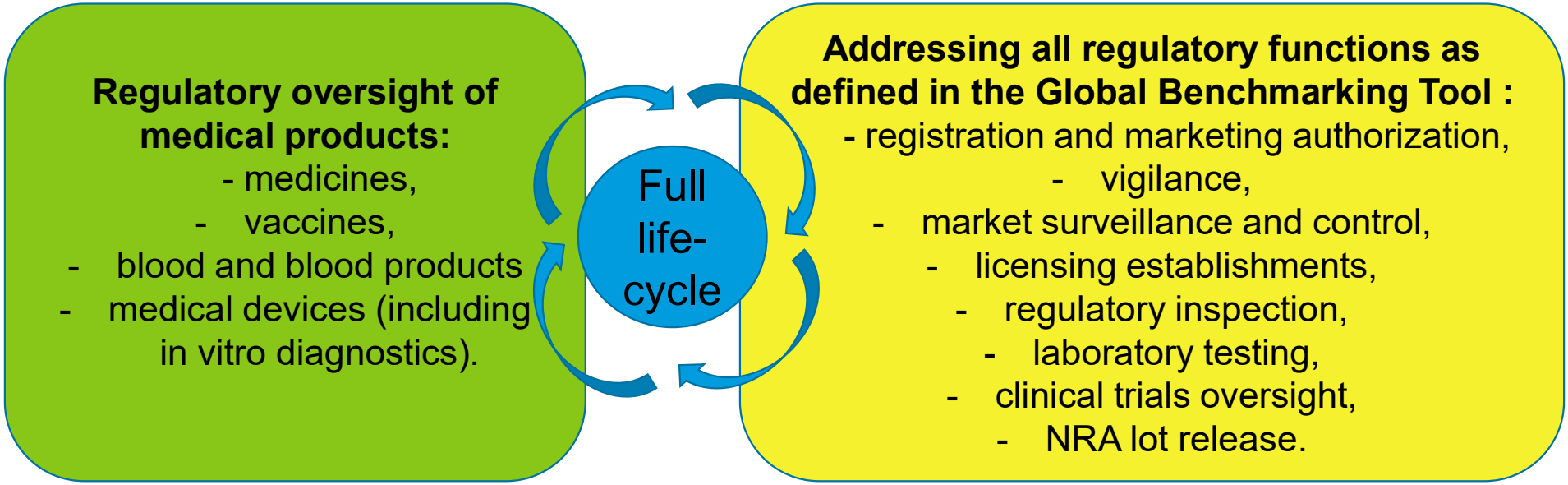
International cooperation essential to ensure the safety, quality and efficacy/performance of locally used medical products.
No regulatory authorities even the best resourced one can do it alone.

Make best use of available resources and expertise, avoid duplication and concentrate regulatory efforts and resources where most needed.
Promote a more efficient approach to regulatory oversight, thereby improving access to quality-assured, effective and safe medical products over the entire life-cycle.

The act whereby the regulatory authority in one jurisdiction takes into account and give significant weight to assessments performed by another regulatory authority or trusted institution, or to any other authoritative information in reaching its own decision.
Various forms of reliance approaches.

The relying authority remains independent, responsible and accountable regarding the decisions taken, even when it relies on the decisions, assessments and information of others.

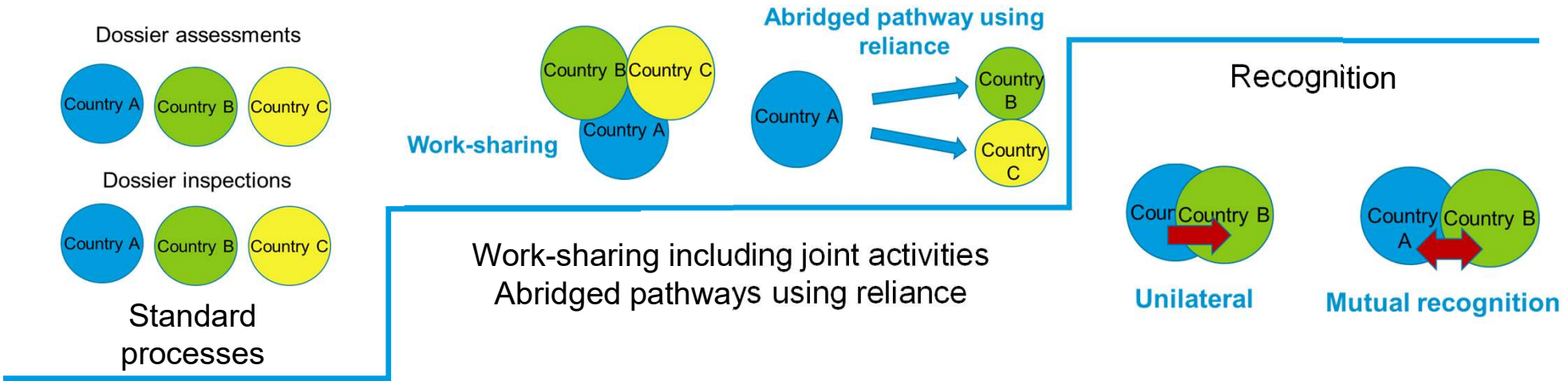
WHO Good Reliance Practices - Scope



WHO Good reliance practices in the regulation of medical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations: Fifty-fifth report. Technical Report Series, No. 1033, Annex 10; 2021. Link: https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations

The high-level document will be complemented in a second step **by an interactive repository of practical examples of reliance and questions and answers documents**

Key concepts of reliance



Independent decisions based on its own reviews and/or inspections	**Leveraging regulatory work** Performed by other competent and trusted authorities to reduce the workload	**Unilateral or mutual recognition** based on treaties or equivalent

Building trust between NRAs, increasing reliance and efficiency

WHO Good Reliance Practices – Principles

Universality

Applies to all NRAs irrespective of their levels of maturity or resources

Sovereignty of decision-making

NRAs maintain independence, sovereignty and accountability

Transparency

Key enabler to adopting new, more efficient ways of conducting regulatory operations. NRAs to be transparent about their reliance approaches

Respect of national/regional legal basis

Coherent with national/regional frameworks and policies

Consistency

Established for specific and well-defined categories of products and processes

Competency

Build and maintain appropriate competencies and scientific expertise

WHO Good Reliance Practices – Key concepts

Recognition (vs. reliance): more formalized approach to reliance, i.e. recognizes the decisions of another regulatory authority, system or institution, with no additional assessment. Usually requires formal and binding legal provisions.

Unilateral vs. mutual: unilaterally/without reciprocity or mutual recognition based on binding mutual agreements or treaties.

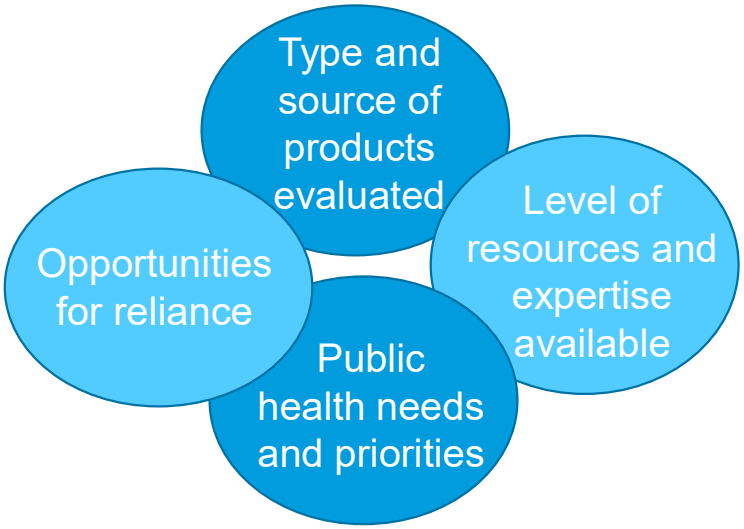
Life cycle approach: to apply across the full life cycle of medical products and all regulatory functions (e.g. important for vigilance and post-authorization activities).

Risk-based approach: NRA to define own strategy (e.g. based on type and source of products evaluated, level of resources and expertise available, public health needs and priorities of the country, and opportunities for reliance) .

Regional reliance mechanisms: assessment for medical products can be conducted centrally based on a regional regulatory system for a group of countries (binding or not).

Risk-based approach

Each NRA should define its **own strategy for an appropriate risk-based approach** to reliance



Using **marketing authorization** as an example, four different reliance based regulatory pathways:

1	2	3	4
Verification of sameness	Confirmation of the applicability of the assessment outcomes	Abridged assessment of data on quality, safety and efficacy or performance	Joint assessment or work-sharing between two or more regulatory authorities
Verification of sameness	Verification of sameness	Verification of sameness	Verification of sameness

WHO Good Reliance Practices – General considerations

- Reliance anchored in a national regulatory authority strategy
- Cultural change
- Flexibility in approach: “one size doesn’t fit all”
- Investment of resources and time in implementing reliance
- “Sameness” of the product in different jurisdictions
- The role of industry
- Reliance in case of a public health emergency

“Sameness” of a product

“two products have identical essential characteristics”

- **All relevant aspects** of drugs, medical devices and in vitro diagnostics to be considered.
- **Results of supporting studies of safety, efficacy and quality**, indications and conditions of use should be the same.
- Impact of **potential, justified differences** to **be assessed** by the manufacturer (and the relying NRA) in determining the possibility of using foreign regulatory assessments/decisions.
- **Essential role of the manufacturer** to confirm the sameness of a product and to provide the same documentation to different NRAs.
- Except for additional country-specific information submitted for review (stability, local label etc.).
- Post-approval changes and vigilance reliance activities as long as the sameness is maintained.

WHO Good Reliance Practices – Barriers and Enablers

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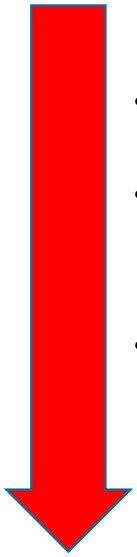

BARRIERS

- Lack of political will
- Lack of accessible information and confidentiality of information
- Other considerations: language, differences in country-specific regulatory requirements, lack of regulatory alignment of product risk-classifications

ENABLERS

- Trust
- Convergence and harmonization
- Information-sharing and dialogue among regulators
- Economic or legal integration
- Engagement of stakeholders

WHO Good Reliance Practices – Examples (Annex)

Clinical Trials, Marketing authorization, Post-approval changes, Testing and lot release, Pharmacovigilance Inspections, Examples in the field of medical devices, Examples in case of public health emergencies

Many examples of Reliance in the Medical Device field – Few examples (1/2)

Abridged Regulatory Pathways

- WHO-Collaborative Registration Procedure for in-vitro diagnostics.

https://www.who.int/publications/m/item/collaborative-procedure-between-the-who-and-nra-s-in-the-assessment-and-accelerated-national-registration-of-who-prequalified-ivd-s-annex4

- Abridged pathways for the approval of medical devices with approval from other regulatory authorities.

Example in Australia, https://www.tga.gov.au/publication/use-market-authorisation-evidence-comparable-overseas-regulators-assessment-bodies-medical-devices-including-ivds, Singapore, https://www.hsa.gov.sg/medical-devices/registration/overview#toggle=togglepanel-overseas-reference-regulatory-agencies

- Reliance pilots happening in different regions for sharing of assessment reports.

Reliance system for a group of countries

Medical Device Single Audit Program (MDSAP), developed under the International Medical Device Regulators Forum (IMDRF): regulatory authorities of Australia, Brazil, Canada, Japan and the USA have pooled their resources into a robust system of oversight by third party auditing organizations, which, in turn, audit the quality management systems of medical device manufacturers.

https://www.fda.gov/medical-devices/cdrh-international-programs/medical-device-single-audit-program-mdsap

Many examples of Reliance in the Medical Device field – Few examples (2/2)

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Work-sharing

The Australia–Canada–Singapore–Switzerland United Kingdom ACCESS Consortium was formed in 2007 by “like-minded” medium-sized regulatory authorities to promote work sharing for greater regulatory collaboration and alignment of regulatory requirements.

Medical devices are under the ACCESS scope of activities.

https://www.tga.gov.au/terms-reference-access-consortium#n8

Mutual Recognition

Manufacturers of medical devices in the European Union (EU) are free to choose a Notified Body that has been designated by a country within the EU to conduct conformity assessment of a medical device product. Once the product is certified, it can be legally placed on any market within the EU.

https://ec.europa.eu/growth/single-market/goods/building-blocks/notified-bodies/

Good Reliance Practices summary

- Reliance as an **essential tool for efficiency of the global regulatory oversight** of medical products.
- Crucial for **regulatory systems strengthening activities**.
- Very important **role of all stakeholders**, including industry, in implementing reliance approaches.

Good Reliance Practices

Thank you

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