WHO Good Regulatory Practices and Good Reliance Practices

World Health Organization

Workshop on Good Regulatory Practices and International Trade - Chile

Wednesday, 27 October 2021

Name of Author | Function | Division | Country

Key Themes of WHO's 13th General Programme of Work 2019-2023

Mission

Promote Health - Keep the World Safe - Serve the Vulnerable

Strategic Priorities

Health Coverage:	1 billion more people with health coverage
Health Emergencies:	1 billion more people made safer
Health Priorities:	1 billion lives improved

Medicines and other Health products (MPH)
Dr. Mariângela SIMÃO, Assistant Director General

DELIVERING QUALITY-ASSURED MEDICAL PRODUCTS FOR ALL

2019–2023

WHO's five-year plan to help build effective and efficient regulatory systems

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Outline

- WHO Regulatory System Strengthening activities
- Good Regulatory Practices Principles
- Good Reliance Practices Principles
- Global Model Regulatory Framework for medical devices including IVDs

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WHO Regulatory System Strengthening activities

Objectives of the WHO regulatory system strengthening programme

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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 GBT

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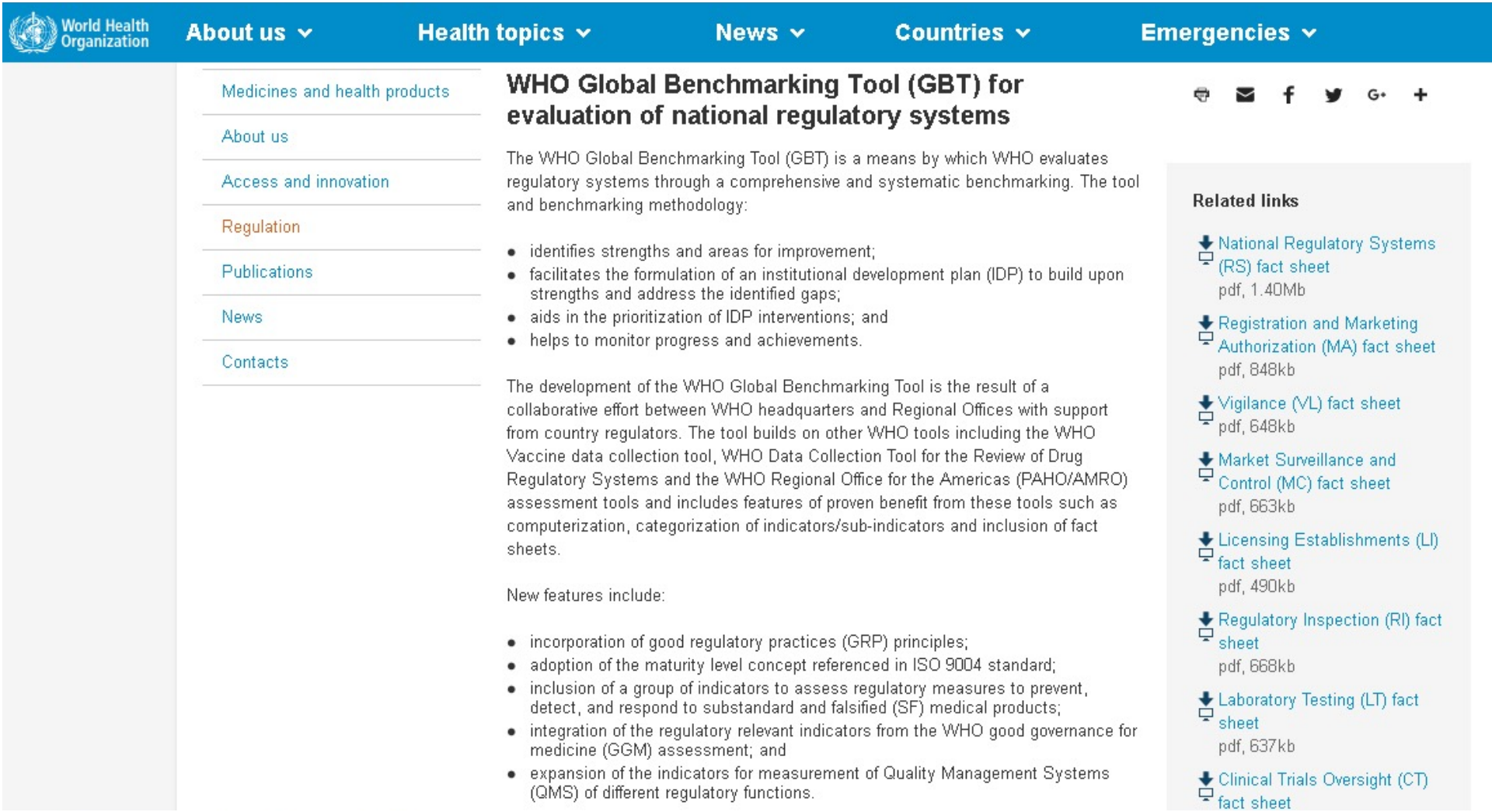

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WHO Global Benchmarking Tool (GBT) for evaluation of national regulatory systems

The WHO Global Benchmarking Tool (GBT) is a means by which WHO evaluates regulatory systems through a comprehensive and systematic benchmarking. The tool and benchmarking methodology:

- identifies strengths and areas for improvement;
- facilitates the formulation of an institutional development plan (IDP) to build upon strengths and address the identified gaps;
- aids in the prioritization of IDP interventions; and
- helps to monitor progress and achievements.

The development of the WHO Global Benchmarking Tool is the result of a collaborative effort between WHO headquarters and Regional Offices with support from country regulators. The tool builds on other WHO tools including the WHO Vaccine data collection tool, WHO Data Collection Tool for the Review of Drug Regulatory Systems and the WHO Regional Office for the Americas (PAHO/AMRO) assessment tools and includes features of proven benefit from these tools such as computerization, categorization of indicators/sub-indicators and inclusion of fact sheets.

New features include:

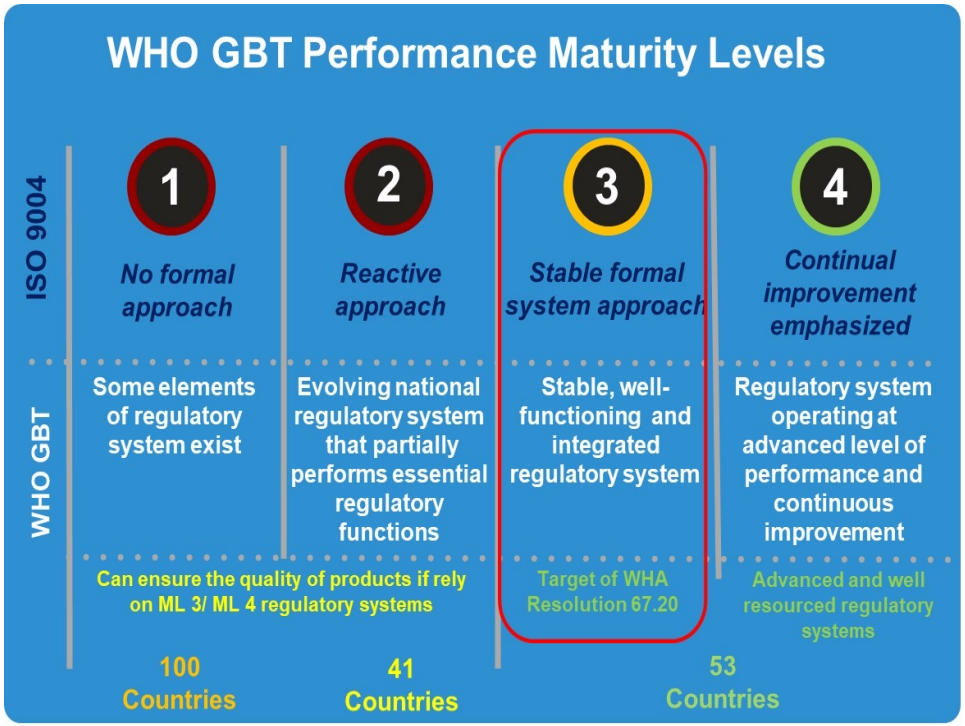
- incorporation of good regulatory practices (GRP) principles;
- adoption of the maturity level concept referenced in ISO 9004 standard;
- inclusion of a group of indicators to assess regulatory measures to prevent, detect, and respond to substandard and falsified (SF) medical products;
- integration of the regulatory relevant indicators from the WHO good governance for medicine (GGM) assessment; and
- expansion of the indicators for measurement of Quality Management Systems (QMS) of different regulatory functions.

Related links

- National Regulatory Systems (RS) fact sheet pdf, 1.40Mb
- Registration and Marketing Authorization (MA) fact sheet pdf, 848kb
- Vigilance (VL) fact sheet pdf, 648kb
- Market Surveillance and Control (MC) fact sheet pdf, 663kb
- Licensing Establishments (LI) fact sheet pdf, 490kb
- Regulatory Inspection (RI) fact sheet pdf, 668kb
- Laboratory Testing (LT) fact sheet pdf, 637kb
- Clinical Trials Oversight (CT) fact sheet

WHO Global Benchmarking Tool (GBT) for evaluation of national regulatory systems of medical products: revision VI

WHO Benchmarking of National Regulatory Authorities (NRAs)



- **The current GBT Rev VI covers only medicines, vaccines and blood and blood products**
- **Revision of the tool to integrate medical devices and IVDs indicators into the GBT was initiated end of last year. The work involved WG members:** WHO, Medical devices and IVDs regulators and laboratory experts and other MDs experts who are non regulators.
- **Discussion :** 1 September 2020 to June 2021.
- **Status:** Editorial work and publishing in Q4.
- **Pilot:** Q1 of 2022

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Good Regulatory Practices Principles

WHO Good Regulatory Practices

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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

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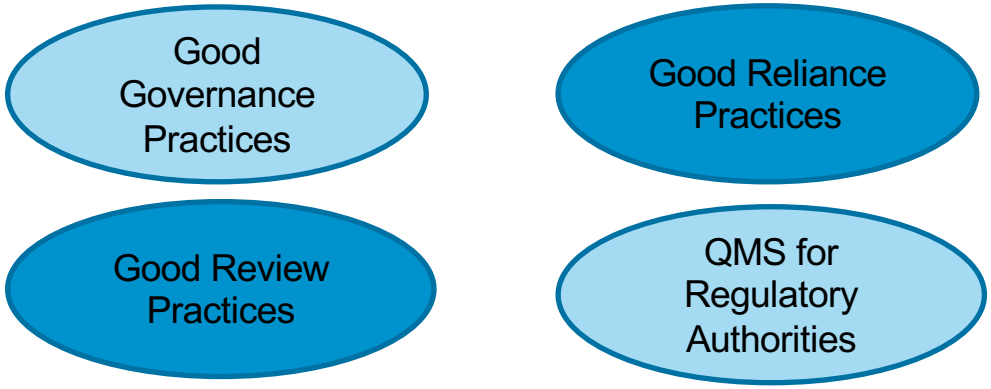
WHO Good Regulatory Practices

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:



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Nine high-level principles

Legality	Consistency	Independence
Impartiality	Proportionality	Flexibility
Clarity	Efficiency	Transparency

GRP main principles

1. Legality

All GRP Principles linked to GBT EXAMPLE

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)

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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

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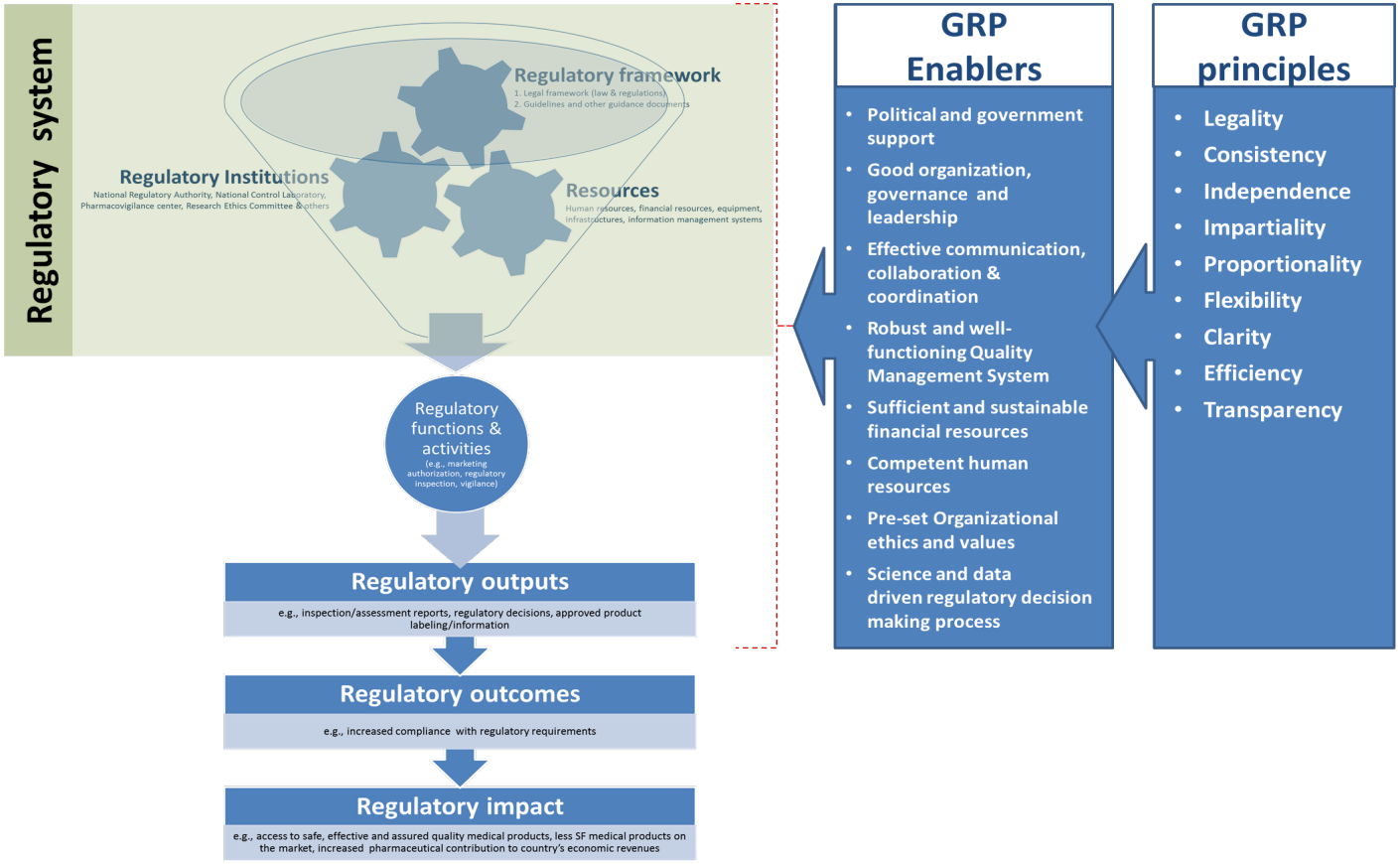

Principles and enablers of Good Regulatory Practices (GRP) and Components of the regulatory system

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Good Reliance Practices Principles

Principles of Reliance

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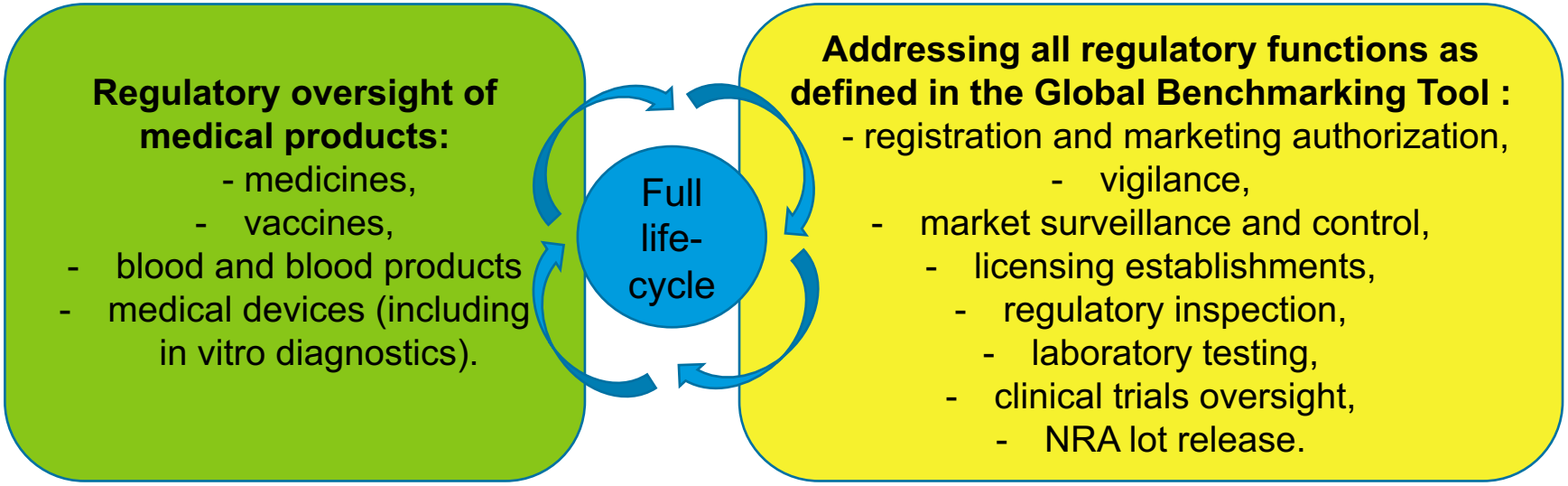
International cooperation essential to ensure the safety, quality and efficacy/performance of locally used medical products.
No regulatory authorities even the best resourced one can do it alone.

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.

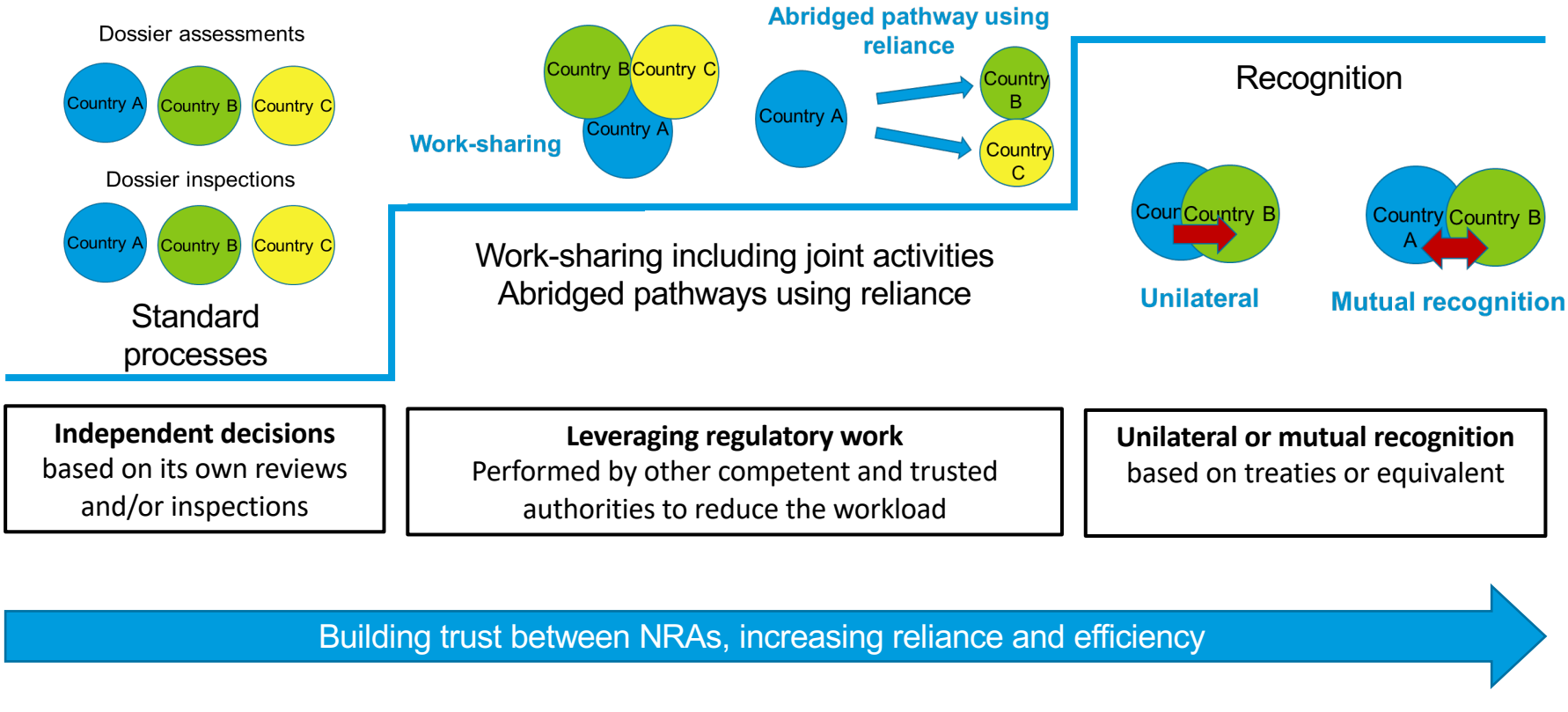
WHO Good Reliance Practices - Scope



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

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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

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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.

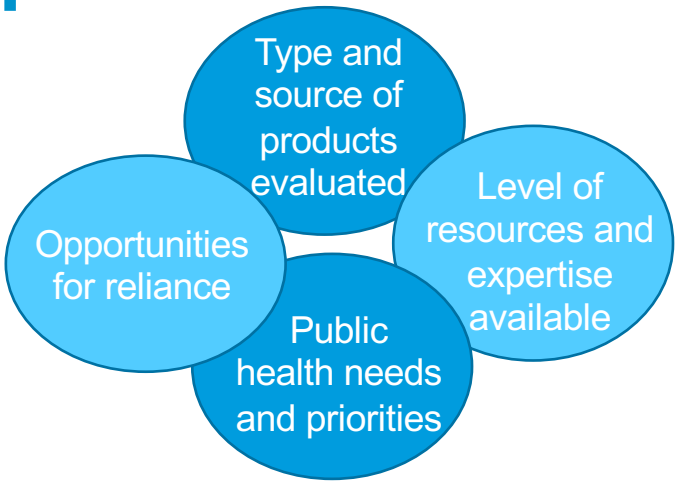
Life cycle approach: to apply across the full life cycle of medical products and all regulatory functions (e.g. important for vigilance and post-authorization activities).

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

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- 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

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“two products have identical essential characteristics”

- **All relevant aspects** medical devices and in vitro diagnostics to be considered.
- **Essential role of the manufacturer** to confirm the sameness of a product and to provide the same documentation to different NRAs.
  - ✓ the same regulatory version;
  - ✓ the same product code(s);
  - ✓ the same site of manufacture and quality management system;
- 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.

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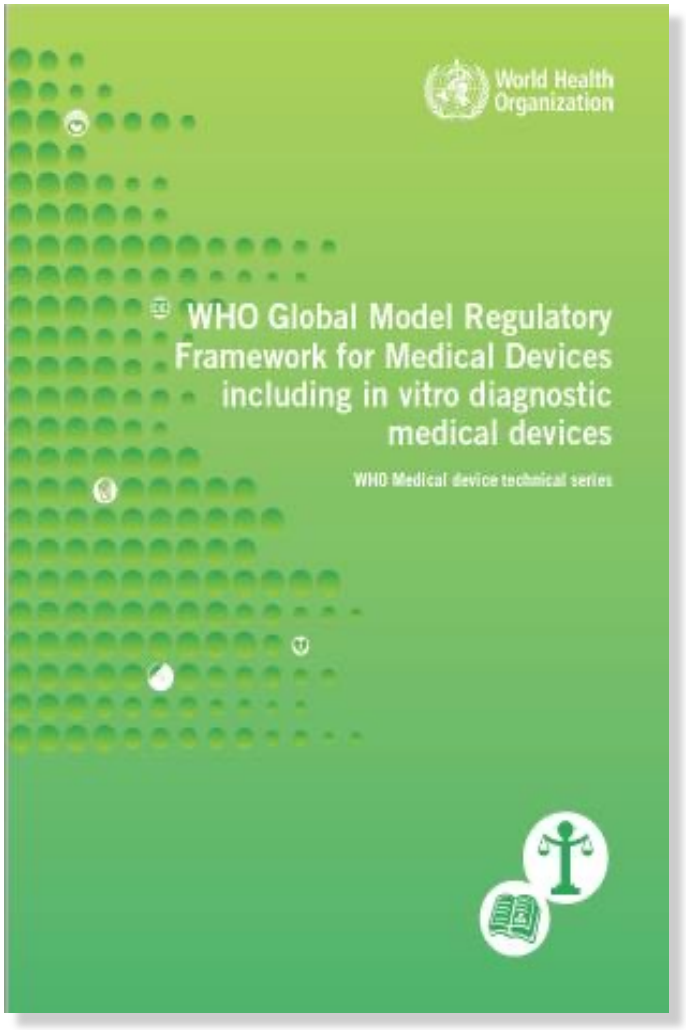
Global Model Regulatory Framework for medical devices including IVDs

The WHO Global Model Regulatory Framework for Medical Devices including IVDs…. Key points



- ✓ Published by WHO in 2017; on going review
- ✓ Relevant for WHO Member States;
- ✓ Recommends two steps i.e. basic regulatory controls towards an expanded level;
- ✓ Describes the role and responsibilities of a country's NRAs for implementing and enforcing the regulations;
- ✓ Describes circumstances in which a regulatory authority may either: "rely on", or "recognize" the work products from trusted regulatory sources

Examples of Reliance in the Medical Device field –

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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

- WHO EUL Facilitated Procedure for SARs CoV-2 assays

https://www.who.int/teams/regulation-prequalification/regulation-and-safety/facilitated-product-introduction/eul-facilitated-procedure

- Thai-FDA - Singapore HSA Regulatory Reliance

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

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;
- To generate quality national decisions regulators globally MUST collaborate and MUST take into consideration the information available from other regulatory authorities;
- Not using the outputs and outcomes from other regulatory authorities means lost opportunity, duplication of efforts, increased regulatory burden and waste of scarce resources.

Thank you

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