WHO Good Reliance Practices (GRelP)

World Health Organization

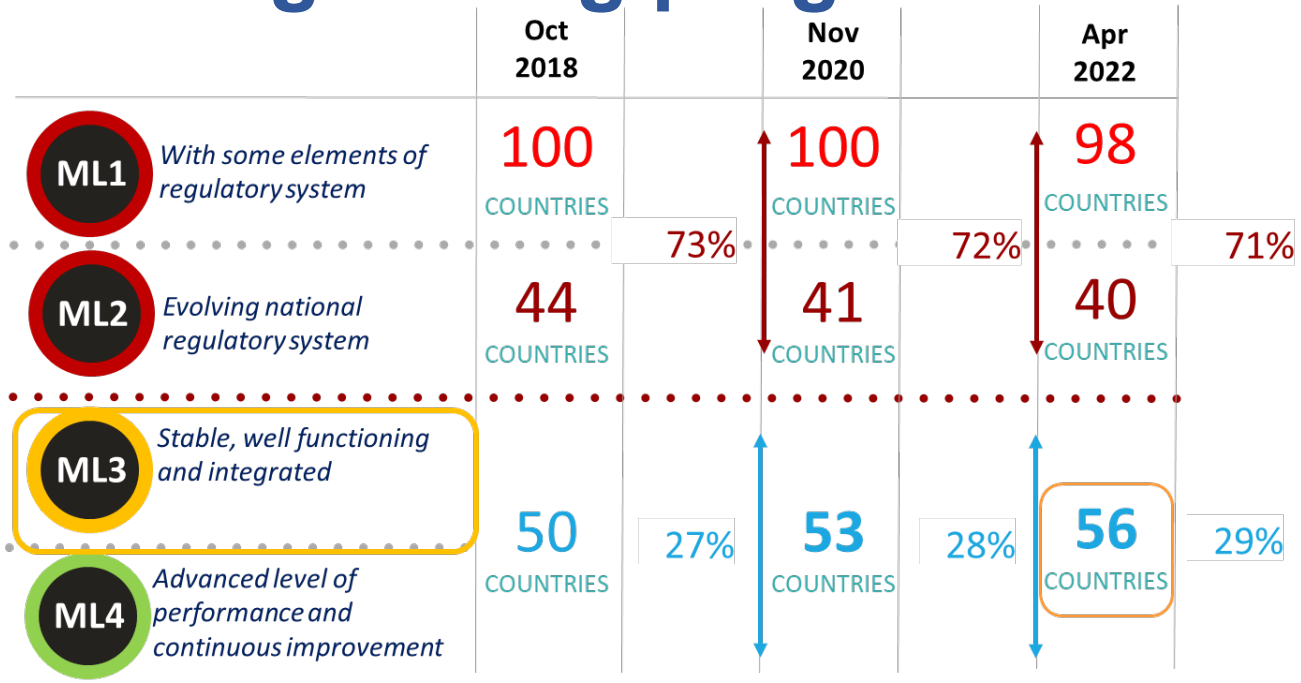
MDRC - PPB Capacity Building Event

24 August 2023

Sunday Kisoma ¦ Consultant ¦ Facilitated Product Introduction

Objectives of the WHO regulatory system strengthening programme

World Health Organization



ML3 **GOAL of WHA Resolution 67.20**

ML: *(regulatory system) maturity level*

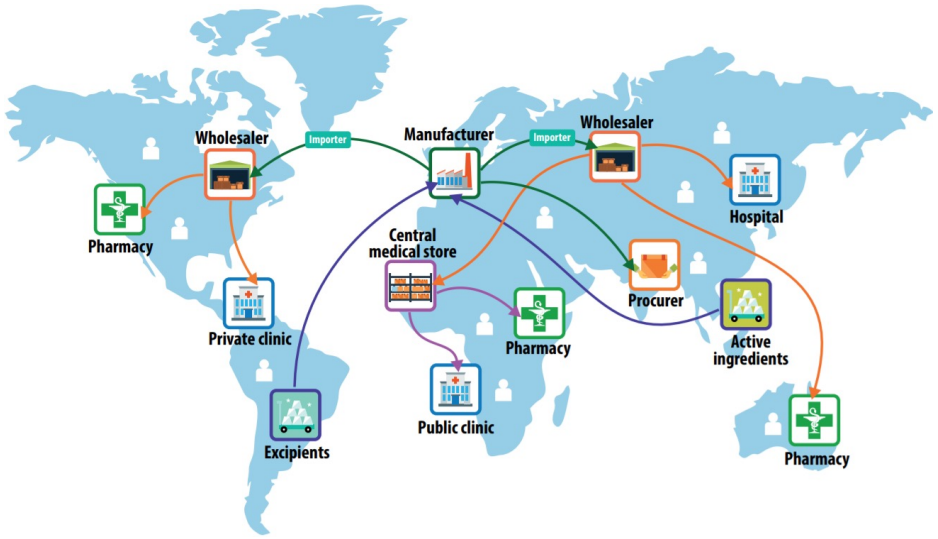
Why reliance?

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

Good regulatory practices, 2021

Good reliance practices, 2021

Evolving Science and Regulatory Challenges



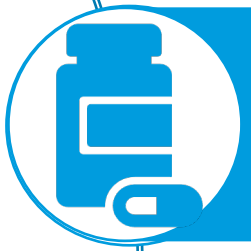
Globalization of markets	Sophistication of health technologies	Rapid evolution of regulatory science
Increasing complexity of supply chains	Transparency and growing public expectations	Lack of global regulatory resources

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.

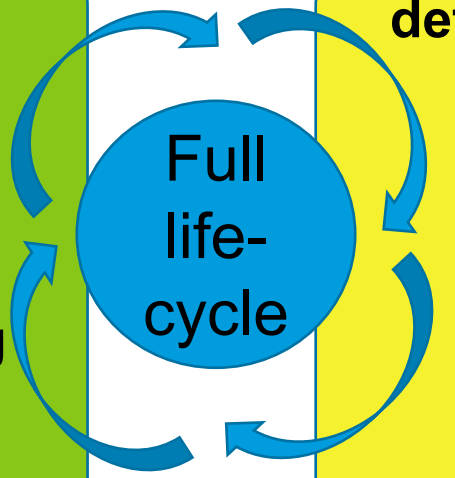
The act whereby the regulatory authority in one jurisdiction takes into account and give significant weight to assessments performed by another regulatory authority or trusted institution, or to any other authoritative information in reaching its own decision.
Various forms of reliance approaches.

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

Regulatory oversight of medical products:

- medicines,
- vaccines,
- blood and blood products
- medical devices (including in vitro diagnostics).



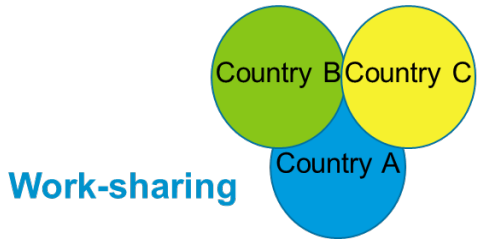
Addressing all regulatory functions as defined in the Global Benchmarking Tool :

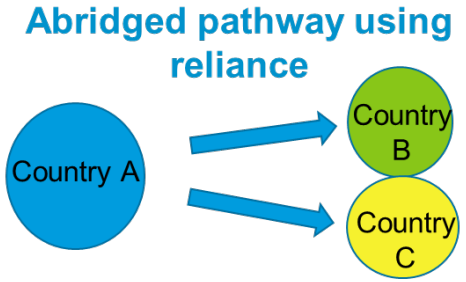
- registration and marketing authorization,
- vigilance,
- market surveillance and control,
- licensing establishments,
- regulatory inspection,
- laboratory testing,
- clinical trials oversight,
- NRA lot release.

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**

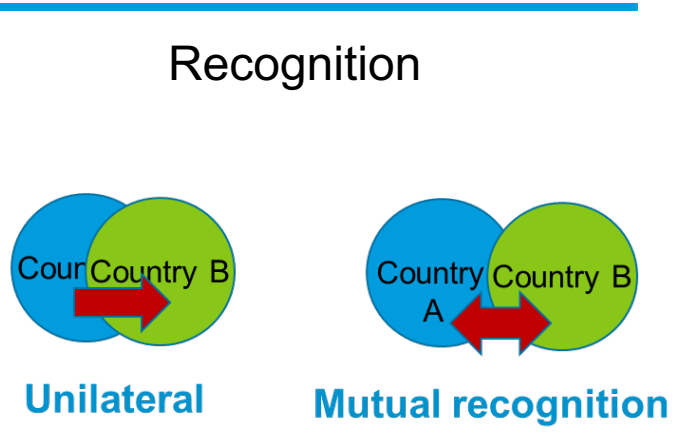
Key concepts of reliance

Standard processes





Work-sharing including joint activities
Abridged pathways using 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: an essential building block of a regulatory system

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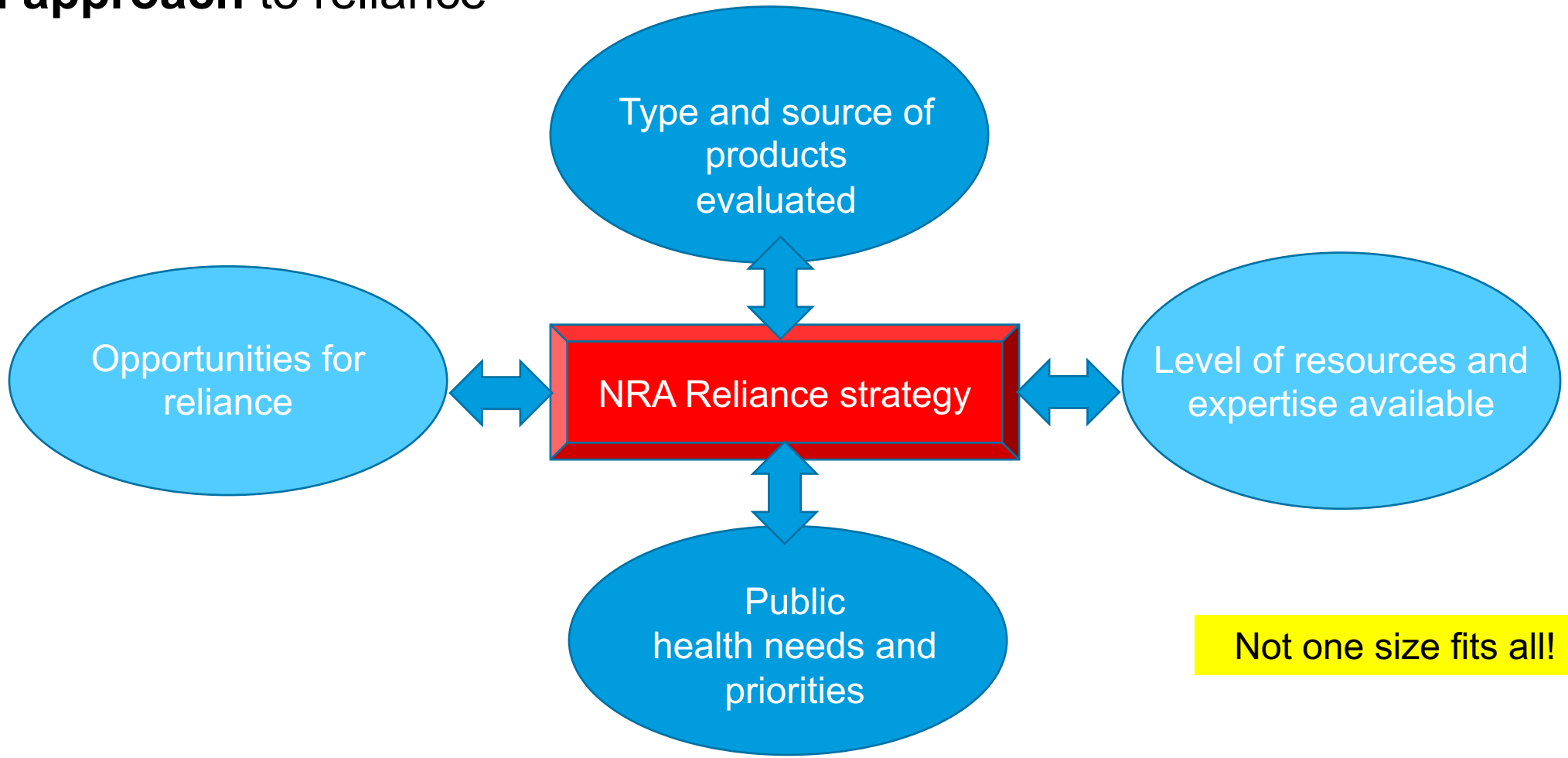
“Regulatory systems with fewer resources can be as effective as those with more resources if they **use a risk-based approach**, take advantage **of the work and decisions of other regulatory authorities** and **focus their resources on essential, value-added activities that can be provided only by the regulatory Authority"**

Risk-based approach: NRA strategy

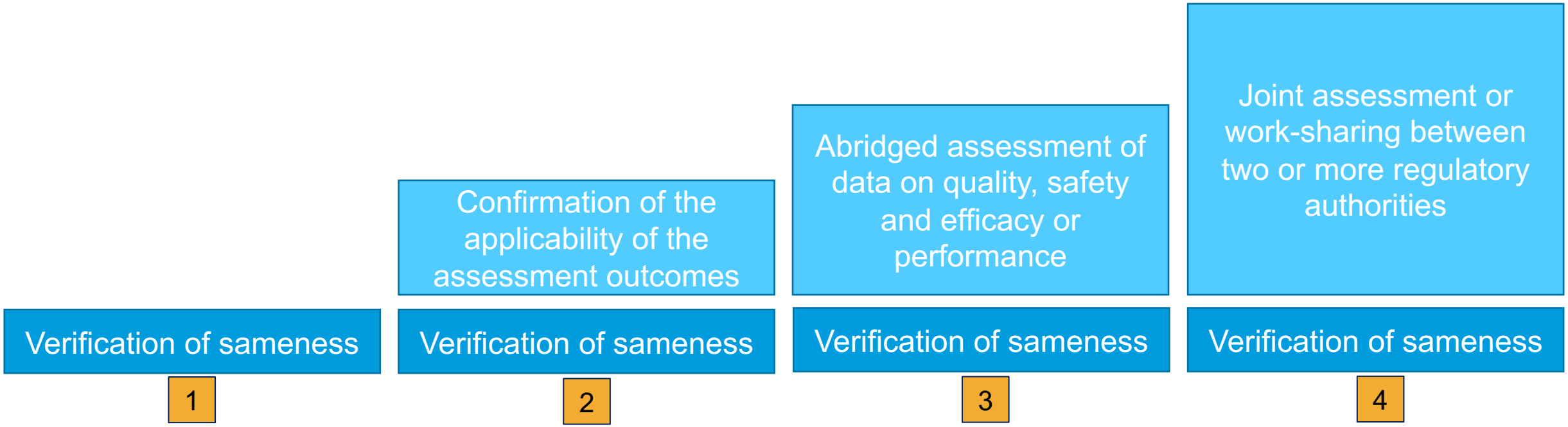
Each NRA should define its **own strategy for an appropriate risk-based approach** to reliance



Not one size fits all!

Risk-based approach for marketing authorizations

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



“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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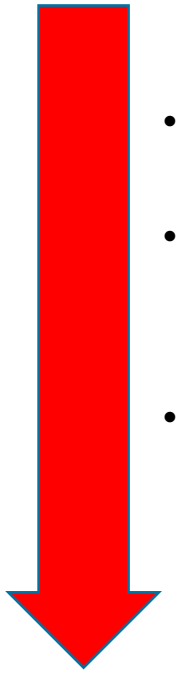
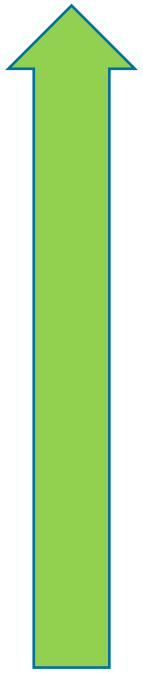


BARRIERS

- 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

Regulatory pathways involving reliance

MAIN PRINCIPLES:

- **Sharing information / expertise** (assessment, inspection and testing results or expertise) that serve as basis for authornational decisions – avoiding duplication.
- **Voluntary participation** – reference authorities, participating ities and manufacturers/sponsors

WHO PQ collaborative registration procedure

Vaccines: 2004

- Medicines: Started in 2012
- Diagnostics: Pilot 2019
- Vector control: Pilot 2020

"SRA" collaborative registration procedure

Initiated in 2015

- European Medicines Agency (EMA)
- UK Medicines and Healthcare Products Regulatory Agency (MHRA)
- 20 African NRAs

Regional networks

African Medicines Regulatory Harmonization Project (AMRH)

ASEAN SIAHR Project

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

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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

- 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/

How can reliance help in case of public health emergency? Few examples

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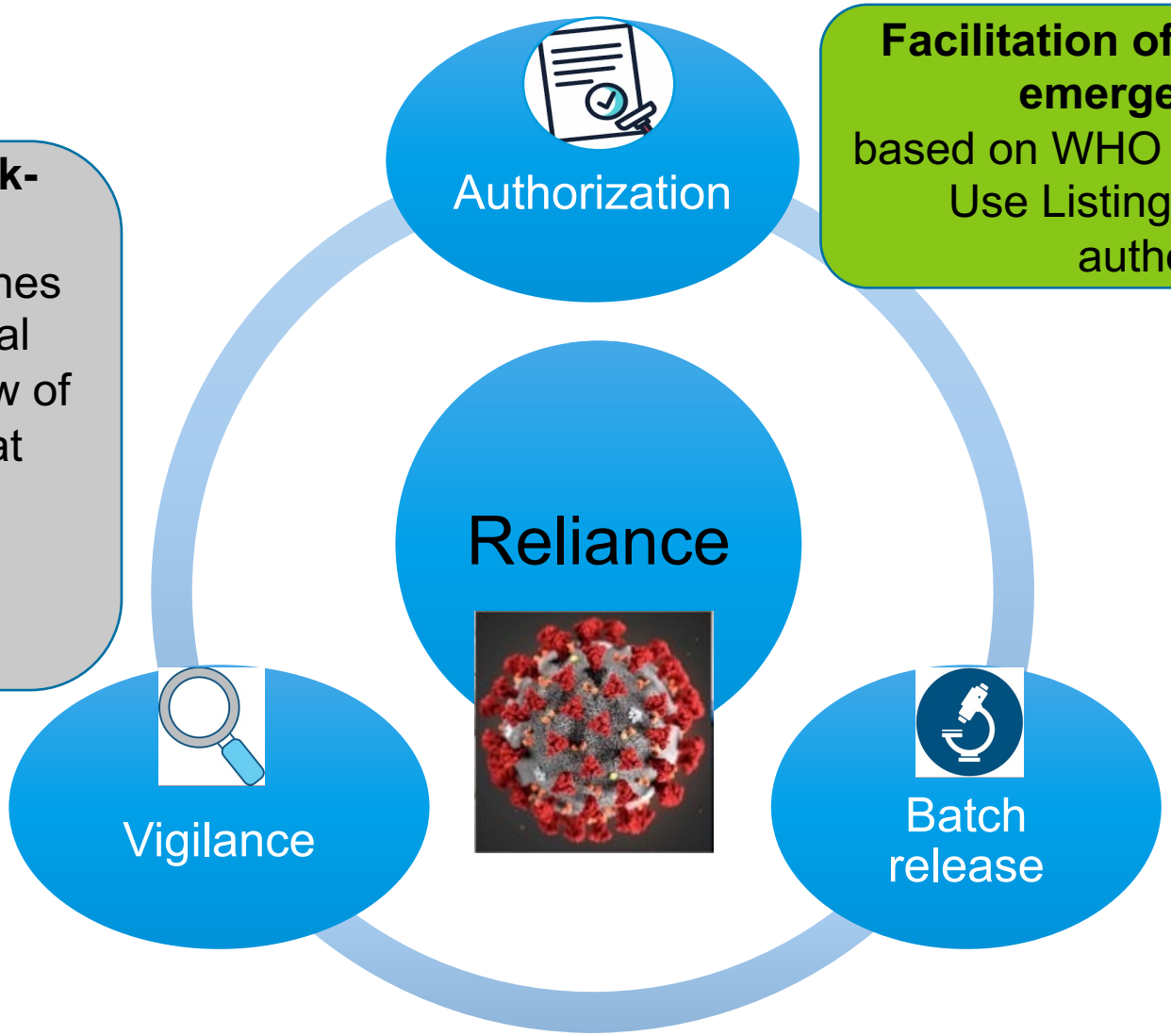
Use of reliance and work-sharing encouraged
(e.g. WHO Covid-19 vaccines safety surveillance manual encourages reliance, review of risk management plans at regional and WHO prequalification level, pharmacovigilance inspections, etc.)



Facilitation of authorization for use or emergency authorization
based on WHO prequalification Emergency Use Listing or stringent regulatory authorities approvals

Avoid retesting of vaccines **through reliance on the batch release testing from releasing NRAs/NCLs** (through the WHO-National Control Laboratory Network for Biologicals)

Good Reliance Practices

Thank you

World Health Organization

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