New developments and challenges on vaccine quality regulation: overview, progress and issues in the region

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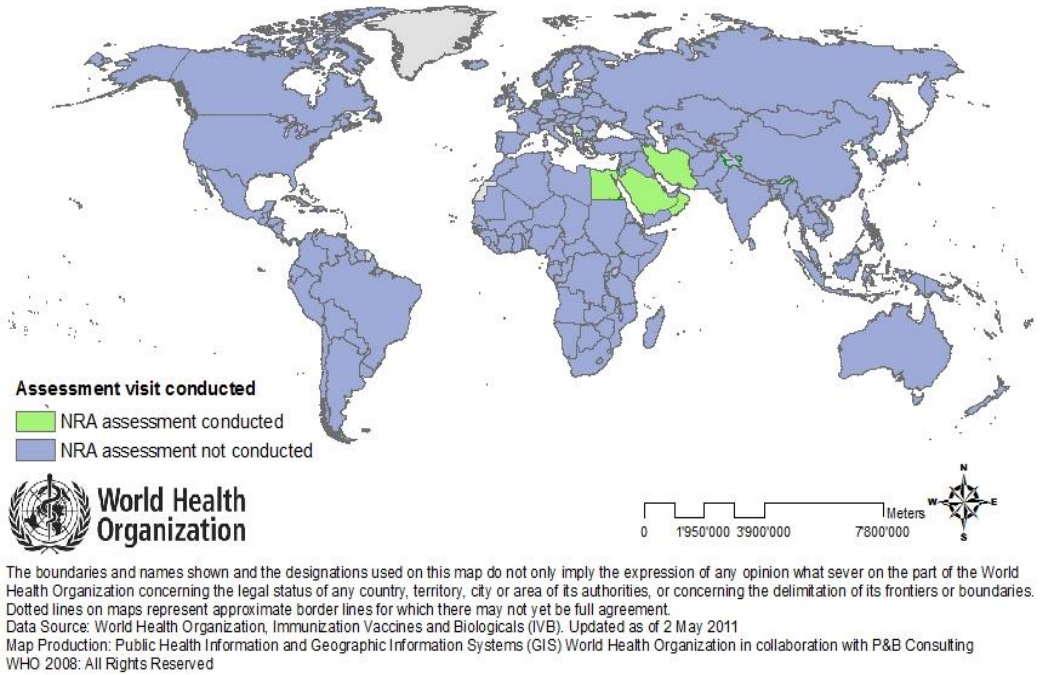
Topics

- New WHO Global Benchmarking Tool
- NRA capacity strengthening and concept of maturity level
- NRA strengthening challenges
- Rationalize NRA capacity strengthening through reliance and recognition
- NRA capacity strengthening priorities in SEARO

WHO NRA Assessment Visits

1997



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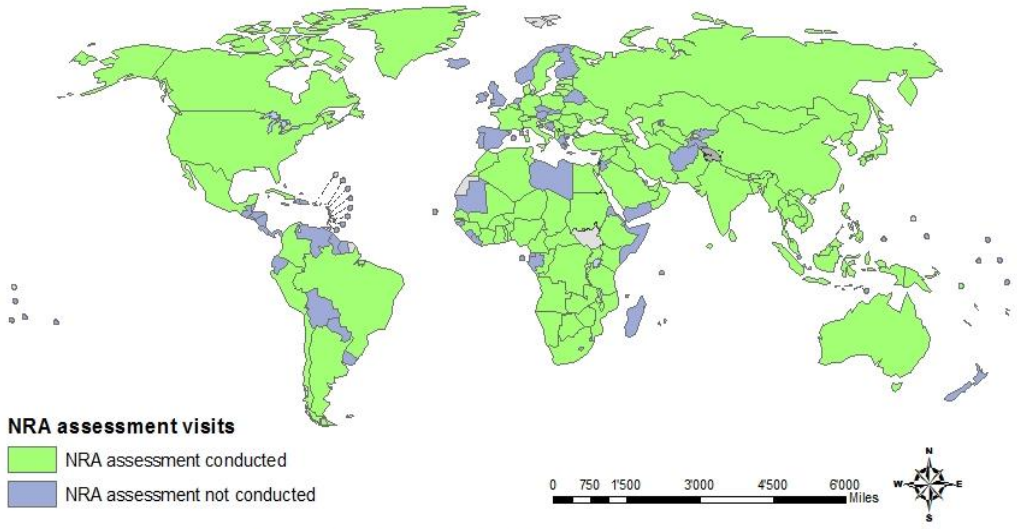
2014



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Key Themes of WHO's 13th GPW 2019-2023

Mission

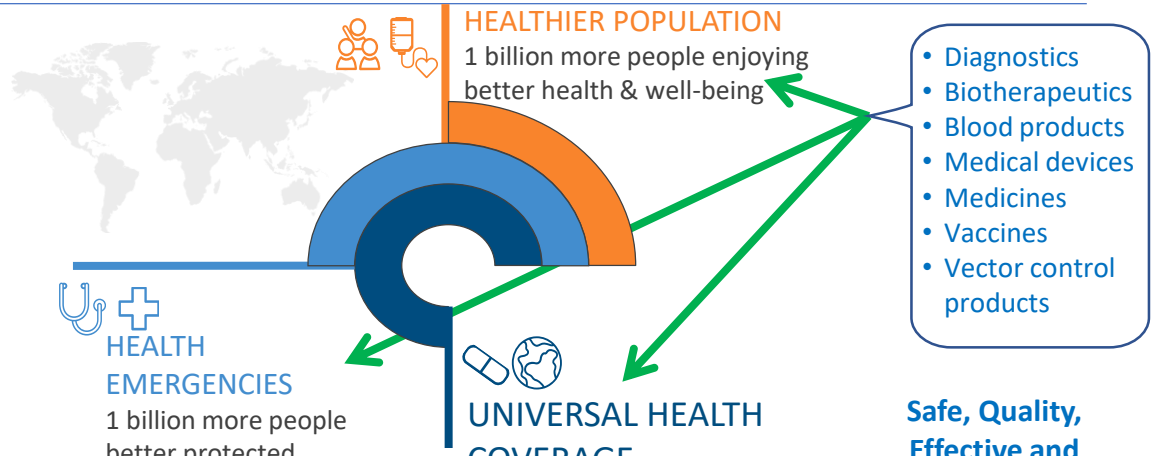
Promote Health - Keep the World Safe - Serve the Vulnerable

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

NEW Cluster	**Access** to Medicines, Vaccines and Pharmaceuticals (MVP)
at EB 2019	Roadmap on **access** to medicines and vaccines http://www.who.int/medicines/access_use/road-map-medicines-vaccines/en/

WHO General Programme of Work - GPW 13

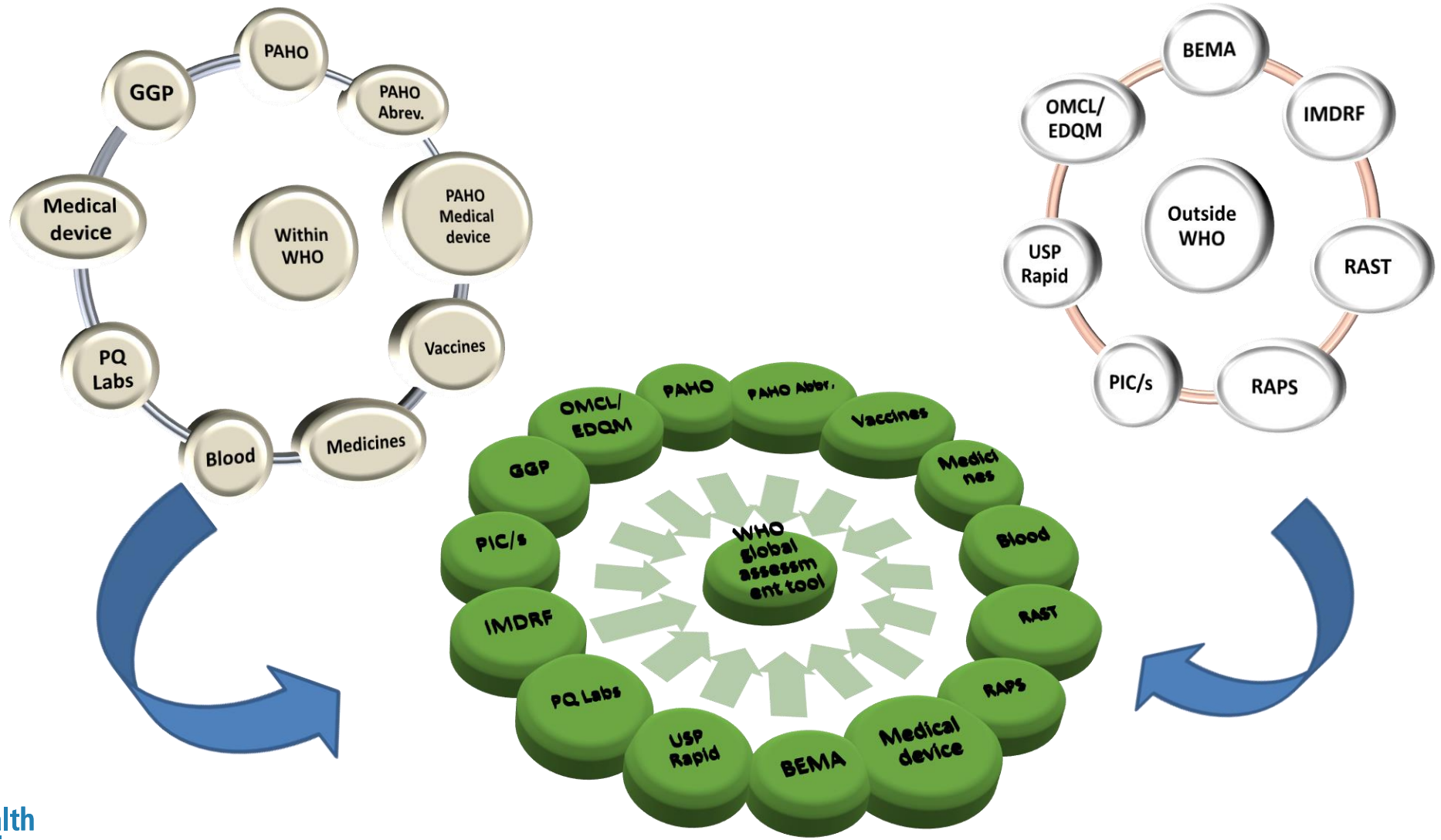


NEW Cluster **Access** to Medicines, Vaccines and Pharmaceuticals (MVP)

at EB 2019 Roadmap on **access** to medicines and vaccines
http://www.who.int/medicines/access_use/road-map-medicines-vaccines/en/

13th WHO Global Programme of Work 2019-2013 calls for a revised NRA Benchmarking tool

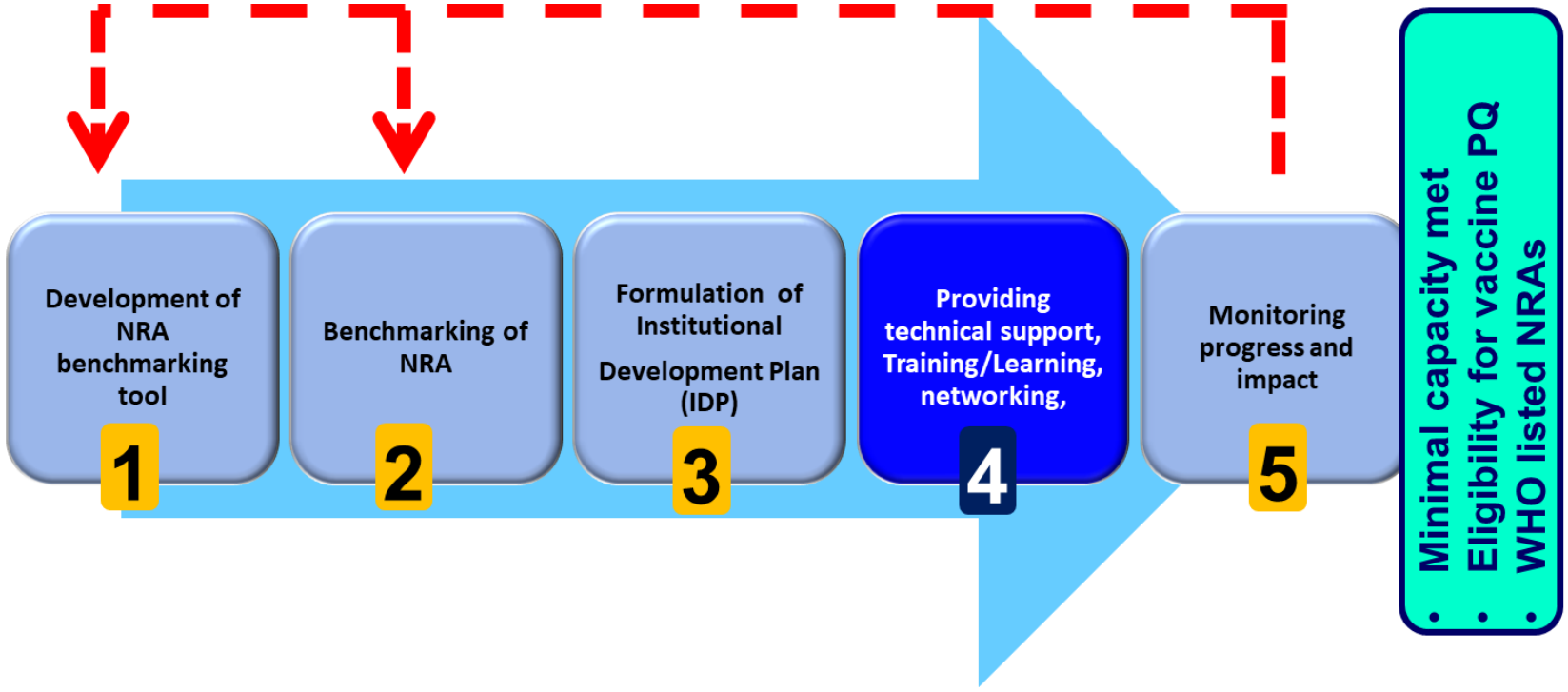
Global context: different assessment tools collecting information from Regulatory Authorities and affiliated institutions



WHO Global Benchmarking Tool for NRA capacity systems

- Initially develop for vaccine regulatory systems, WHO new GBT includes new functions and indicators for safety and quality oversight for medicines and vaccines, but with a view to incorporating other product types in the future.

- WHO NRA capacity strengthening methodology applies the five steps approach.



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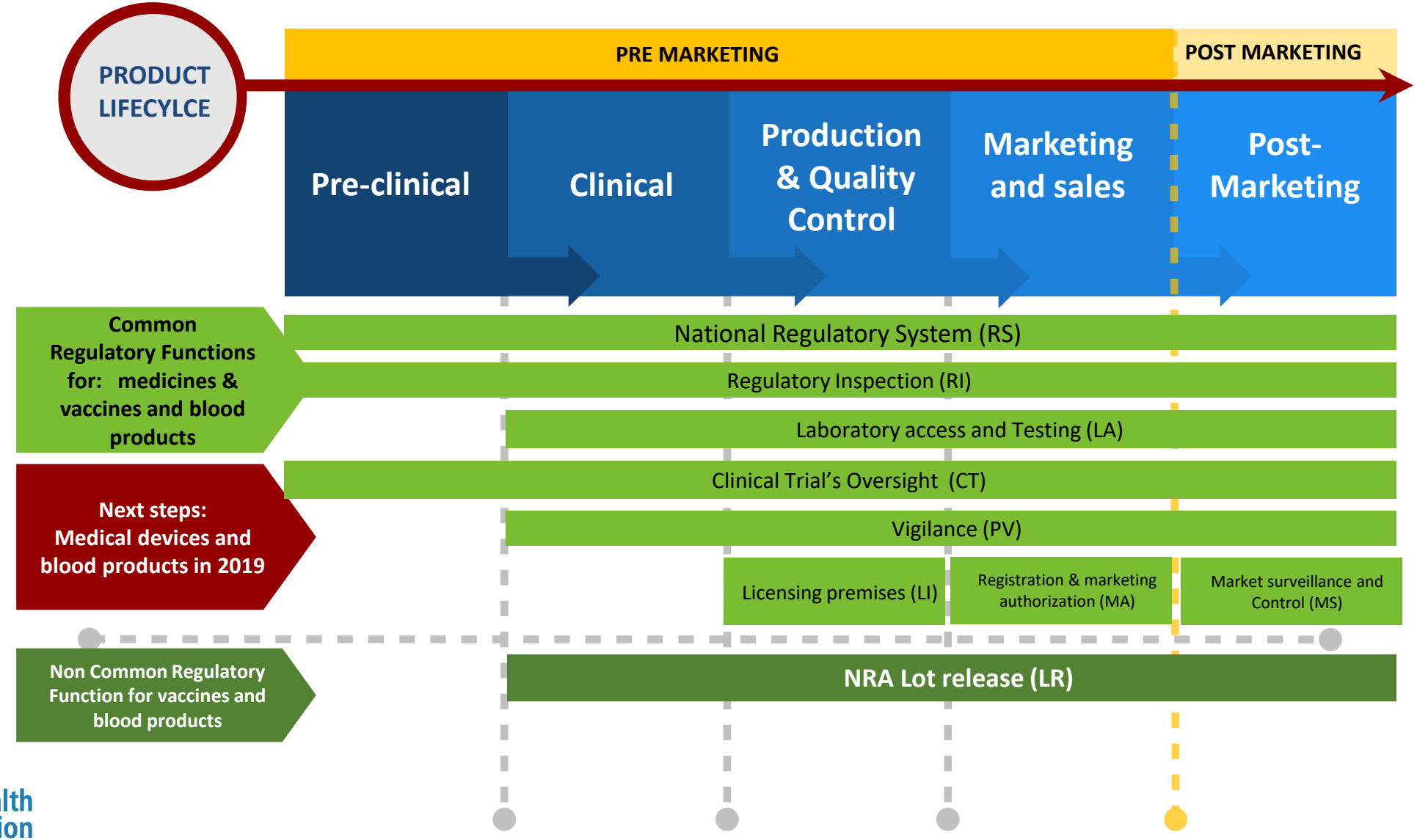
WHO RECOMMENDED REGULATORY FUNCTIONS FOR MEDICINES, VACCINES BASED ON PRODUCT LIFECYCLE



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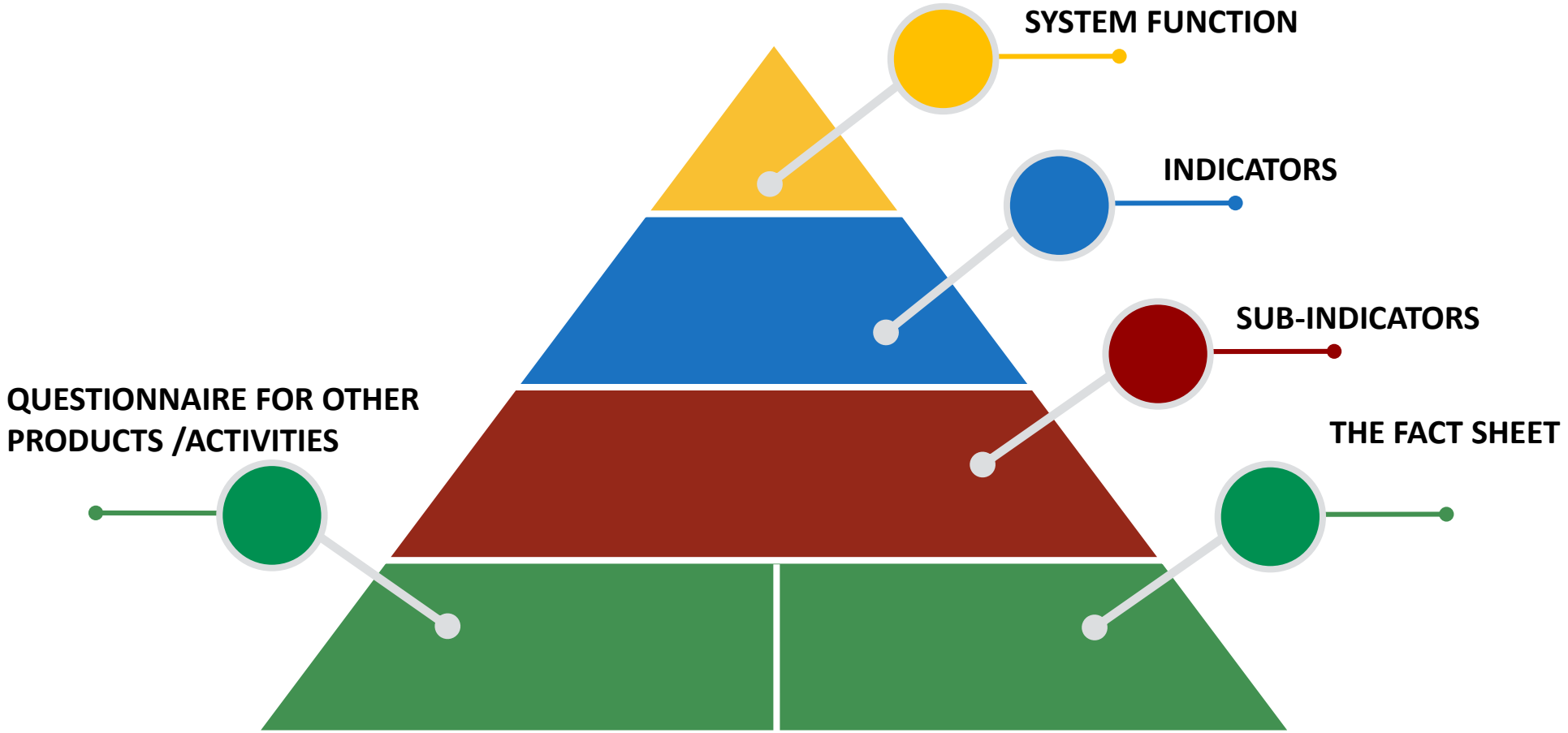
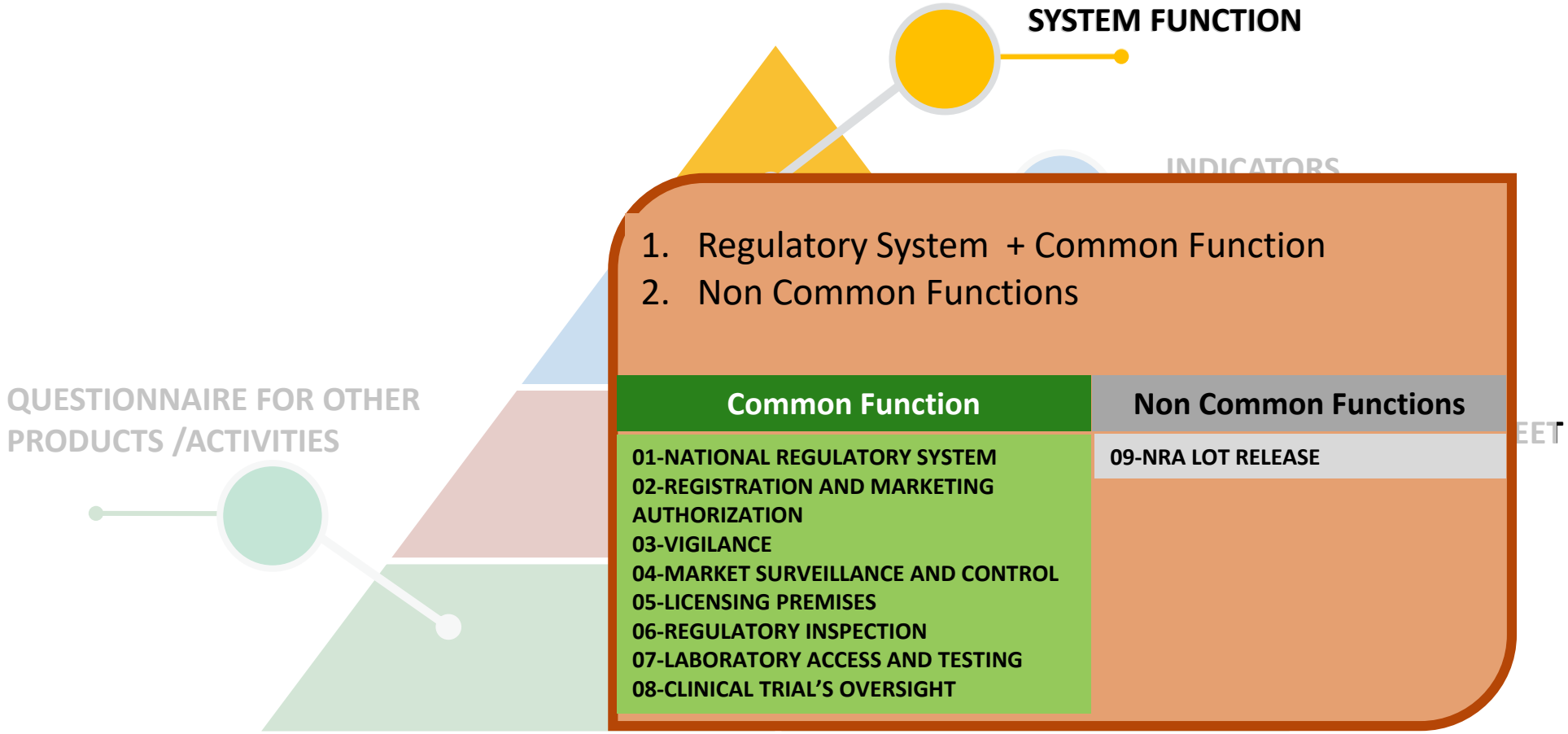
WHO Global Benchmarking Tool

- Structure/Hierarchy



WHO Global Benchmarking Tool

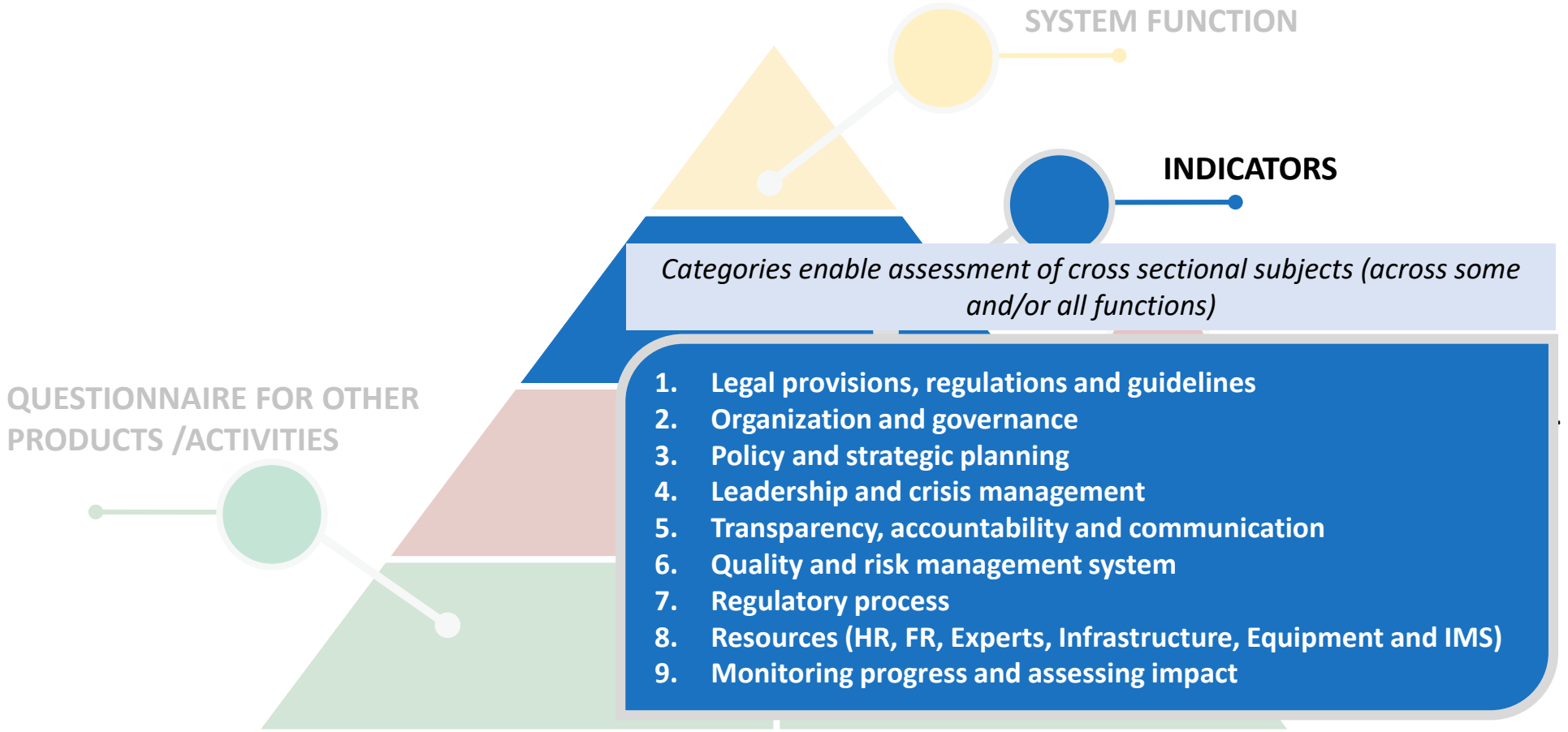
- Structure/Hierarchy



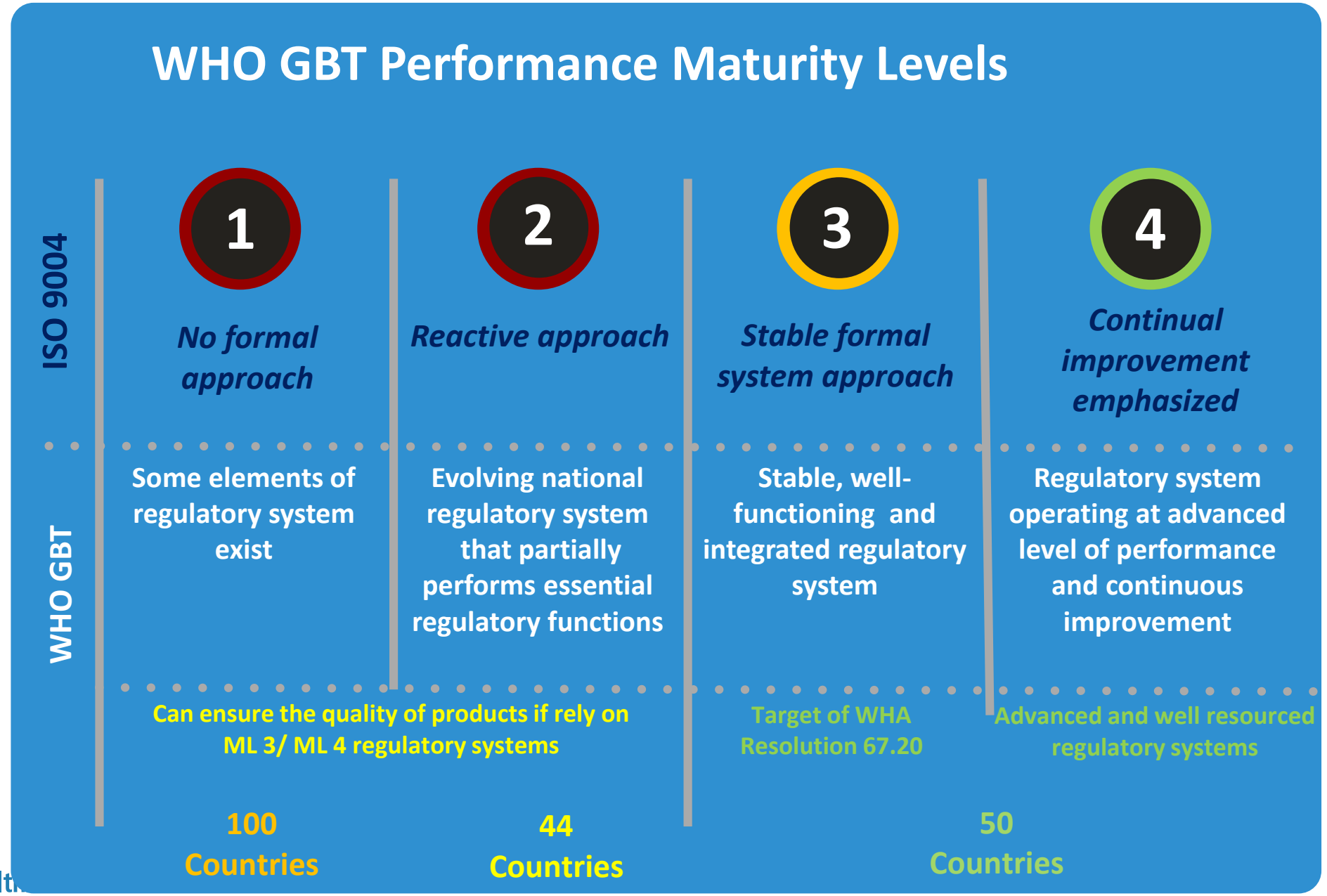
WHO Global Benchmarking Tool

- Structure/Hierarchy

Indicators Categorization (cross cutting subjects)



WHO GBT Performance Maturity Levels



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Updated Figures of the WHO GBT revision VI

Item / Function	RS	MA	VL	MC	LI	RI	LA	CT	LR	Grand Total
Number of Sub-Indicators	60	35	26	27	19	26	28	30	17	268
Sub-Indicators measuring maturity level 1	4	6	5	3	2	3	2	2	1	28
Sub-Indicators measuring maturity level 2	7	2	3	4	1	2	2	8	3	32
Sub-Indicators measuring maturity level 3	27	23	14	15	13	13	18	17	11	152
Sub-Indicators measuring maturity level 4	22	4	4	5	3	8	6	3	2	56

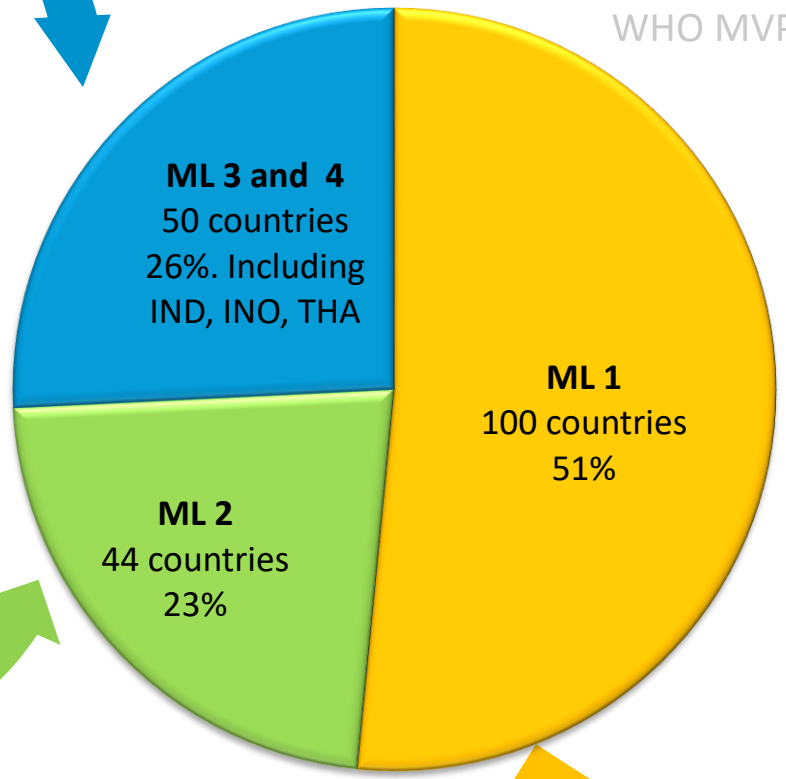
Minimal capacity

Advanced/reference NRAs

Regulatory systems' maturity level in SEAR

GBT in IND (2017), INO & THA (2018) show Mat3 and above for the three countries.

(Updated 8 Feb 2019)
WHO MVP/RSS/CRS



Self-assessment in BAN 2017 and SRL 2018.

- **BAN multi –year plan to reach Mat 3 and above by 2020**
- **SRL formal assessment in Oct 2019**

GBT assessment in DPRK 2018
Technical support for 3 months to finalize GBT, implement IDP and strengthen regulatory inspections

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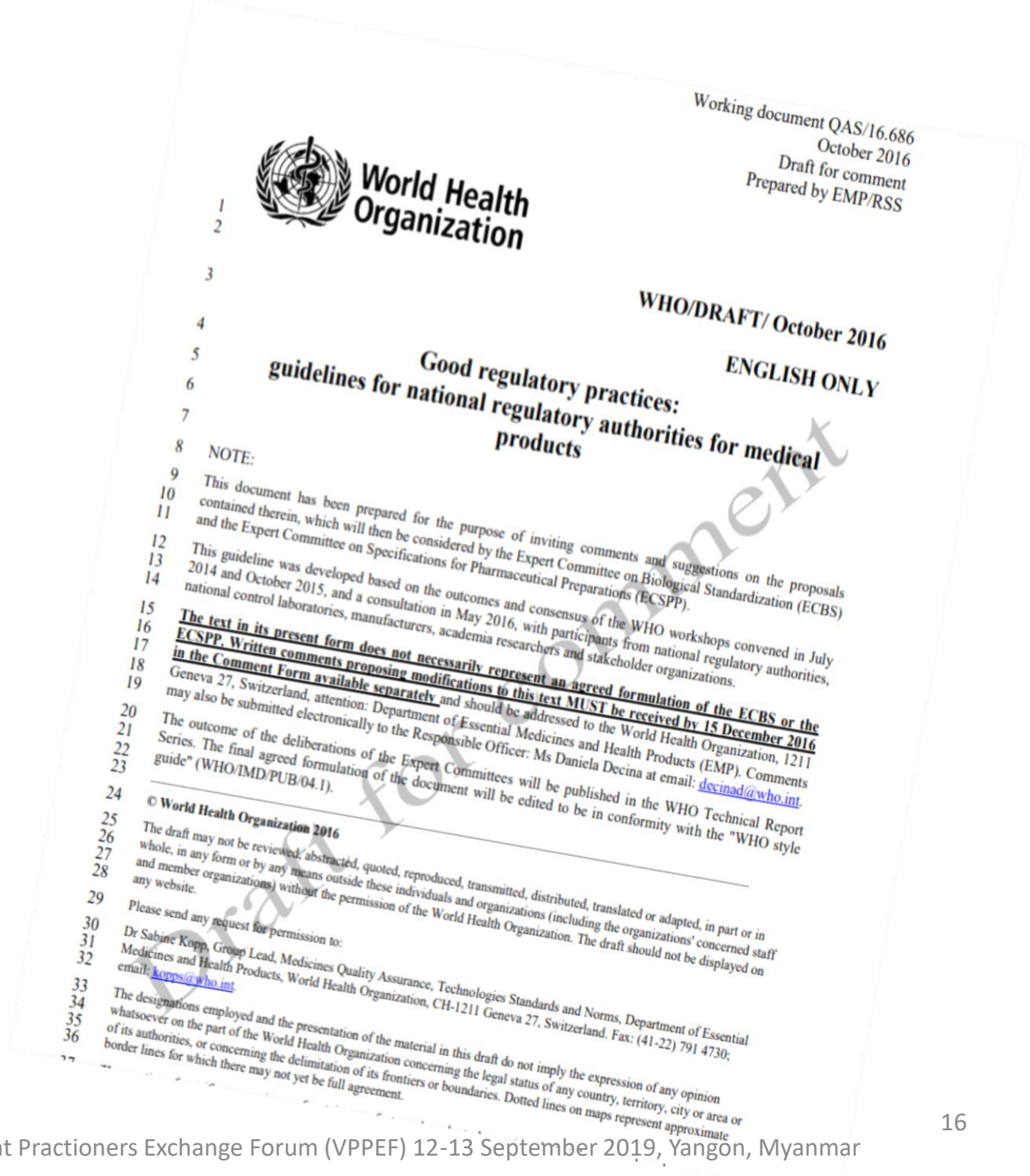
Regulatory challenges

- Regulators face an increasingly complex regulatory environment and need to cooperate
- Need to ensure product quality and supply chain security
- Need to ensure data integrity – can we rely on the data we get to support clinical trials and manufacturing?
- Need to support a global approach to authorization and supervision of medicines
- Need to avoid duplication and help create synergies
- The 4Cs: Communication, Collaboration, Cooperation, Coalitions

Defining reliance

- WHO GRP guideline offers helpful 2-step definition of reliance:
  1) take into account (part or fully) assessment done by others
  2) retain responsibility for your own decision



Working document QAS/16.686
October 2016
Draft for comment
Prepared by EMP/RSS

World Health Organization

WHO/DRAFT/ October 2016

ENGLISH ONLY

Good regulatory practices: guidelines for national regulatory authorities for medical products

NOTE:

This document has been prepared for the purpose of inviting comments and suggestions on the proposals contained therein, which will then be considered by the Expert Committee on Biological Standardization (ECBS) and the Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP).

This guideline was developed based on the outcomes and consensus of the WHO workshops convened in July 2014 and October 2015, and a consultation in May 2016, with participants from national regulatory authorities, national control laboratories, manufacturers, academia researchers and stakeholder organizations.

The text in its present form does not necessarily represent an agreed formulation of the ECBS or the ECSPP. Written comments proposing modifications to this text MUST be received by 15 December 2016 in the Comment Form available separately and should be addressed to the World Health Organization, 1211 Geneva 27, Switzerland, attention: Department of Essential Medicines and Health Products (EMP). Comments may also be submitted electronically to the Responsible Officer: Ms Daniela Decina at email: decinad@who.int.

The outcome of the deliberations of the Expert Committees will be published in the WHO Technical Report Series. The final agreed formulation of the document will be edited to be in conformity with the "WHO style guide" (WHO/IMD/PUB/04.1).

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Dr Sabine Kopp, Group Lead, Medicines Quality Assurance, Technologies Standards and Norms, Department of Essential Medicines and Health Products, World Health Organization, CH-1211 Geneva 27, Switzerland. Fax: (41-22) 791 4730; email: kopps@who.int.

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Draft for comment

Definitions

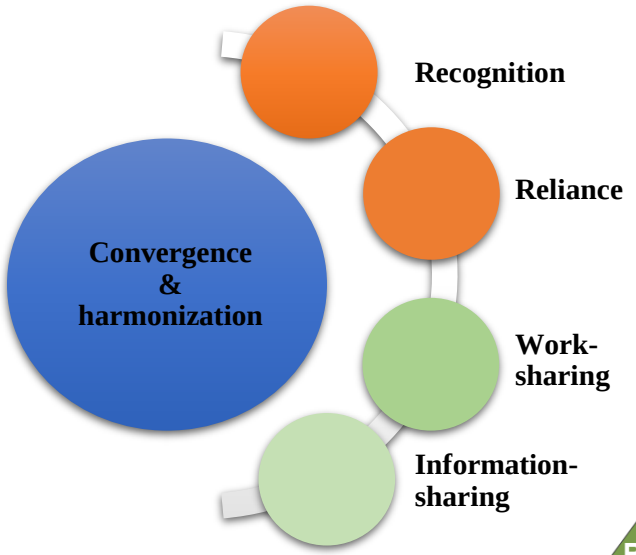
- **Reliance:**

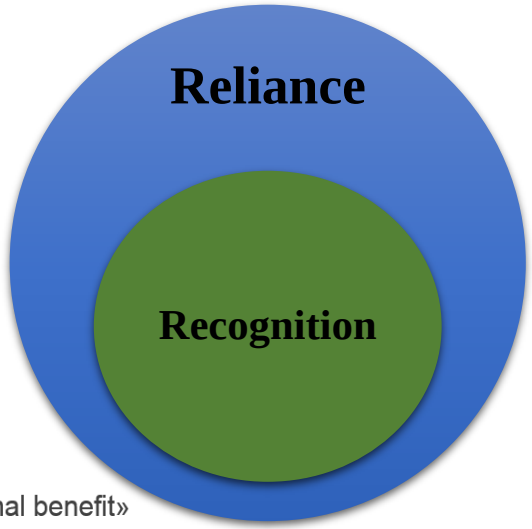
  act whereby a regulatory authority in one jurisdiction may take into account/give significant weight to work performed by another regulator or other trusted institution in reaching its own decision.

- **Recognition:**

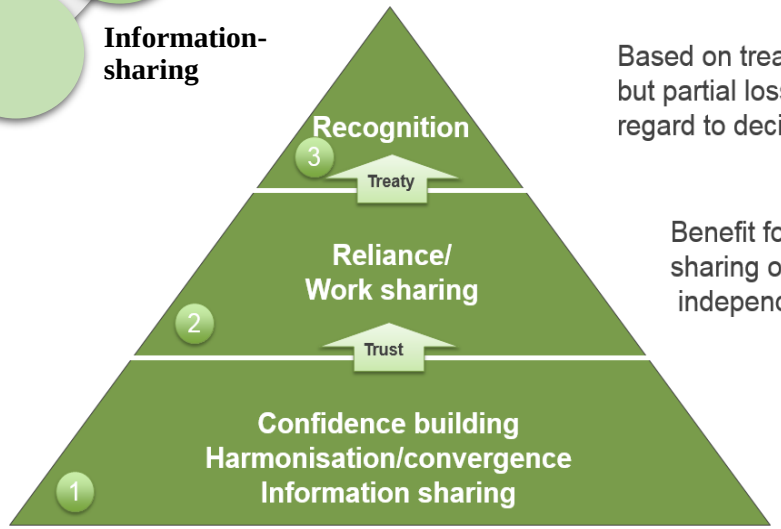
  the routine acceptance of the regulatory decision of another regulator or other trusted institution. Recognition indicates that evidence of conformity with the regulatory requirements of country A is sufficient to meet the regulatory requirements of country B.

Views on Reliance and Recognition





Based on treaties; «maximal benefit» but partial loss of sovereignty with regard to decision-making



Benefit for regulators; sharing of workload, but independent decisions

«Foundation», Equivalence of requirements

Reliance example #1: IGDRP

- International Generic Drugs Regulatory Programme https://www.ema.europa.eu/en/documents/other/international-generic-drug-regulators-programme-information-sharing-pilot_en.pdf
- Pilot launched in 2012
- Uses EU decentralised procedure as model for sharing of generic products information among IGDRP authorities external to EU.
- Under the pilot arrangements, the assessment reports generated by the EU CP would be shared with collaborating IGDRP agencies outside EUs.

Reliance example #2: WHO

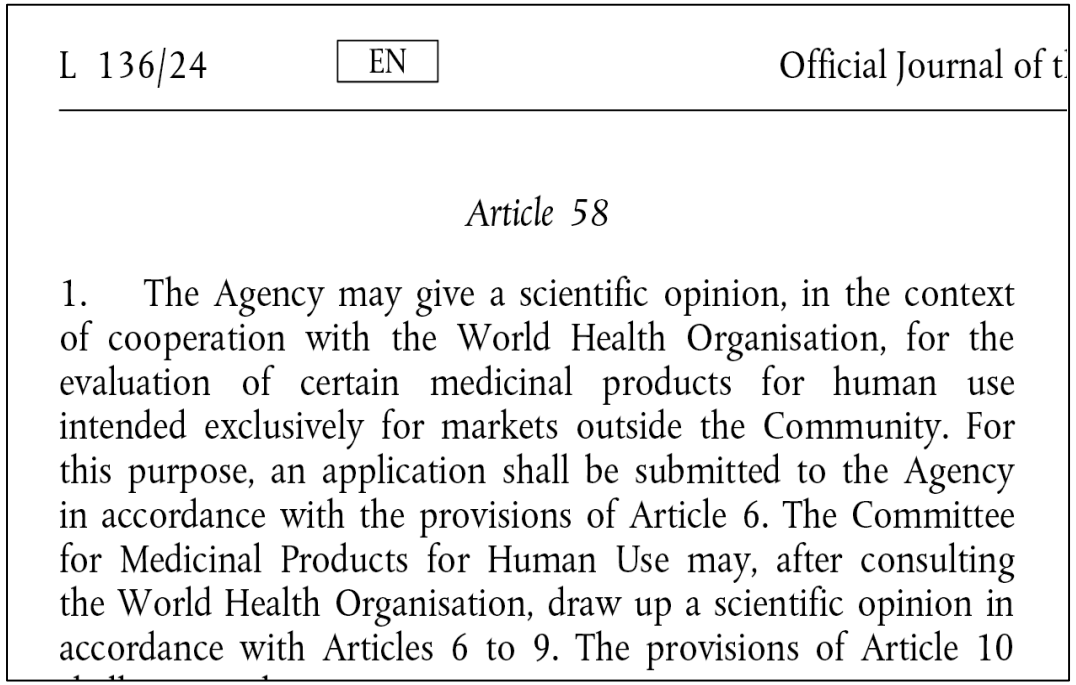
WHO Collaborative Registration: https://apps.who.int/medicinedocs/documents/s22405en/s22405en.pdf aims to:

- provide convenient tool for NRAs wishing to enhance their premarketing evaluation and registration system by taking advantage of the scirntific assessment work conducted by WHO?PQT
- accelerate the approval process based on the EMA assessment, while allowing competent authorities which might have limited regulatory resources to fulfil their regulatory responsibilities and make their own decisions.

The procedure is not applicable to pharmaceutical products that have been listed as prequalified on the bais of approval by stringent NRA.

Reliance example #3: Article 58

- Introduced as a tool to help to expand LMIC access to new medicines and improve public health
- Promotes reliance through:
  - Involvement of experts/observers from 'target country' NRAs
  - Cooperation with WHO



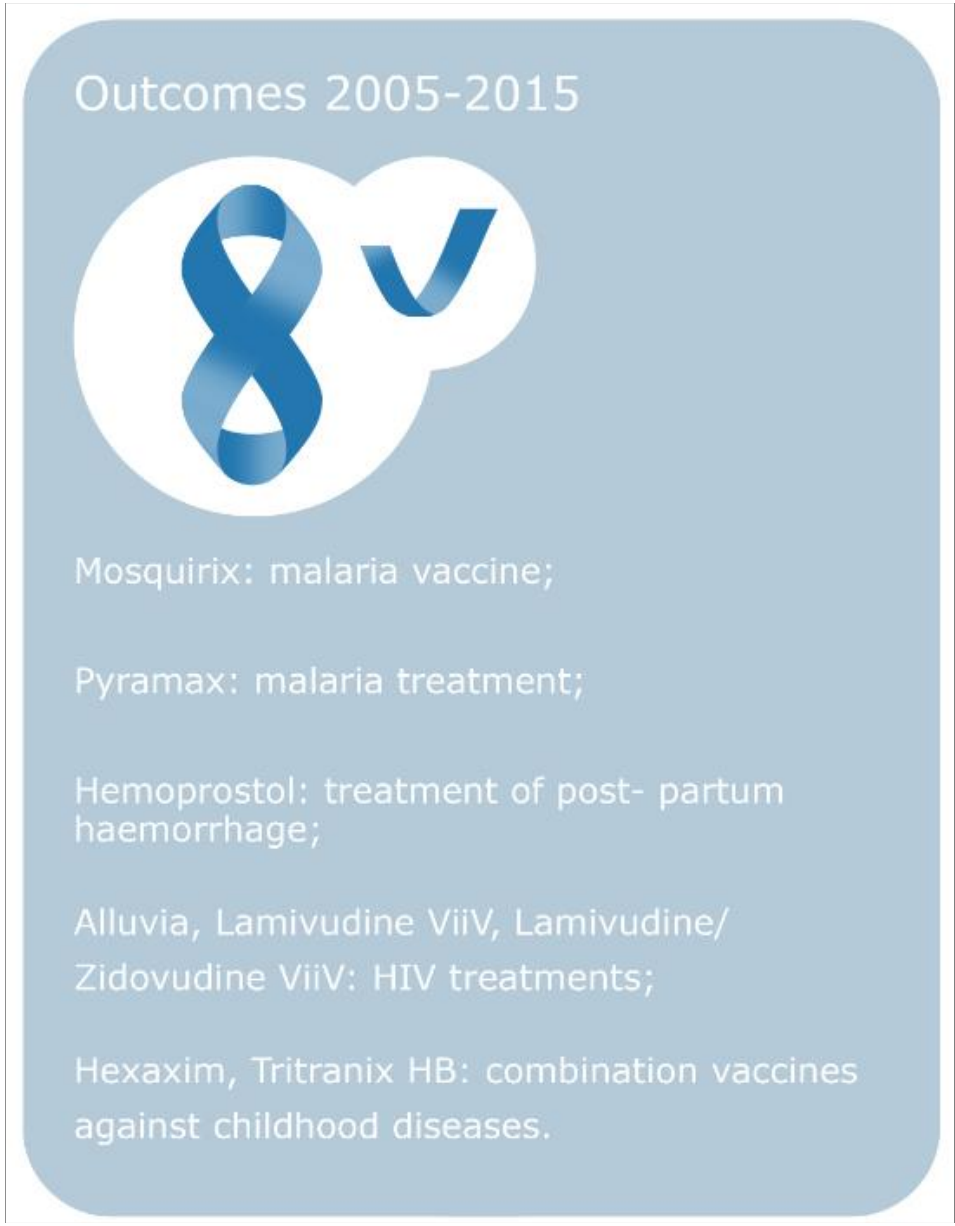
L 136/24 EN Official Journal of t

Article 58

1. The Agency may give a scientific opinion, in the context of cooperation with the World Health Organisation, for the evaluation of certain medicinal products for human use intended exclusively for markets outside the Community. For this purpose, an application shall be submitted to the Agency in accordance with the provisions of Article 6. The Committee for Medicinal Products for Human Use may, after consulting the World Health Organisation, draw up a scientific opinion in accordance with Articles 6 to 9. The provisions of Article 10

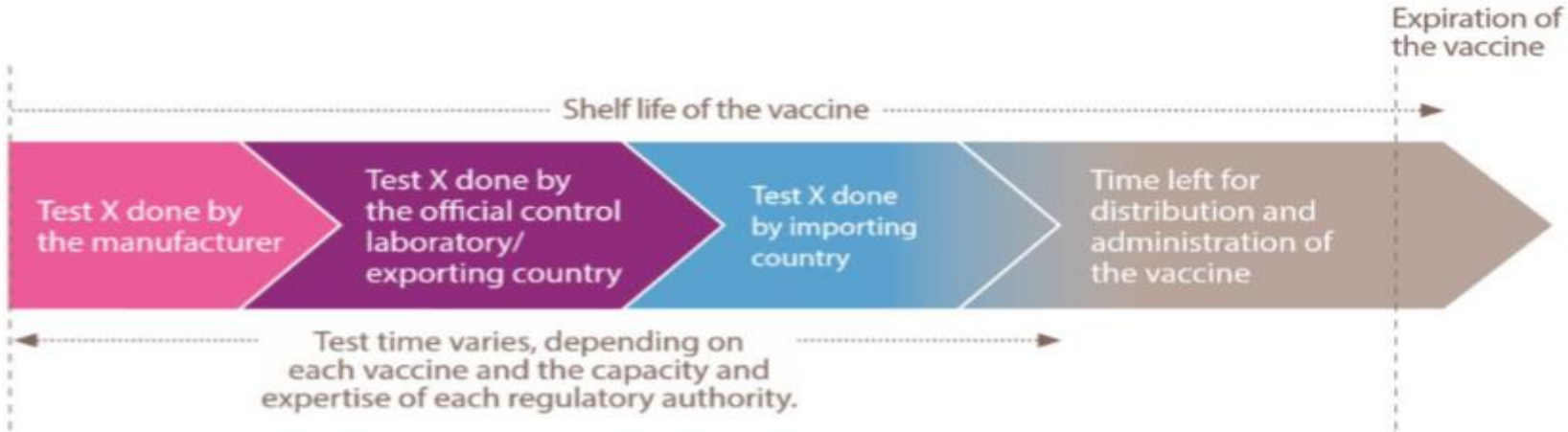
What is Article 58?

- EMA assessment of quality, safety, efficacy of medicine for use outside EU
- Collaboration with WHO + relevant non-EU regulators
- Licensing decision is taken by regulator in country where medicine or vaccine will be used
- Same scientific standards and procedures as for medicines for use in EU
- Benefit-Risk assessment focused on non-EU population



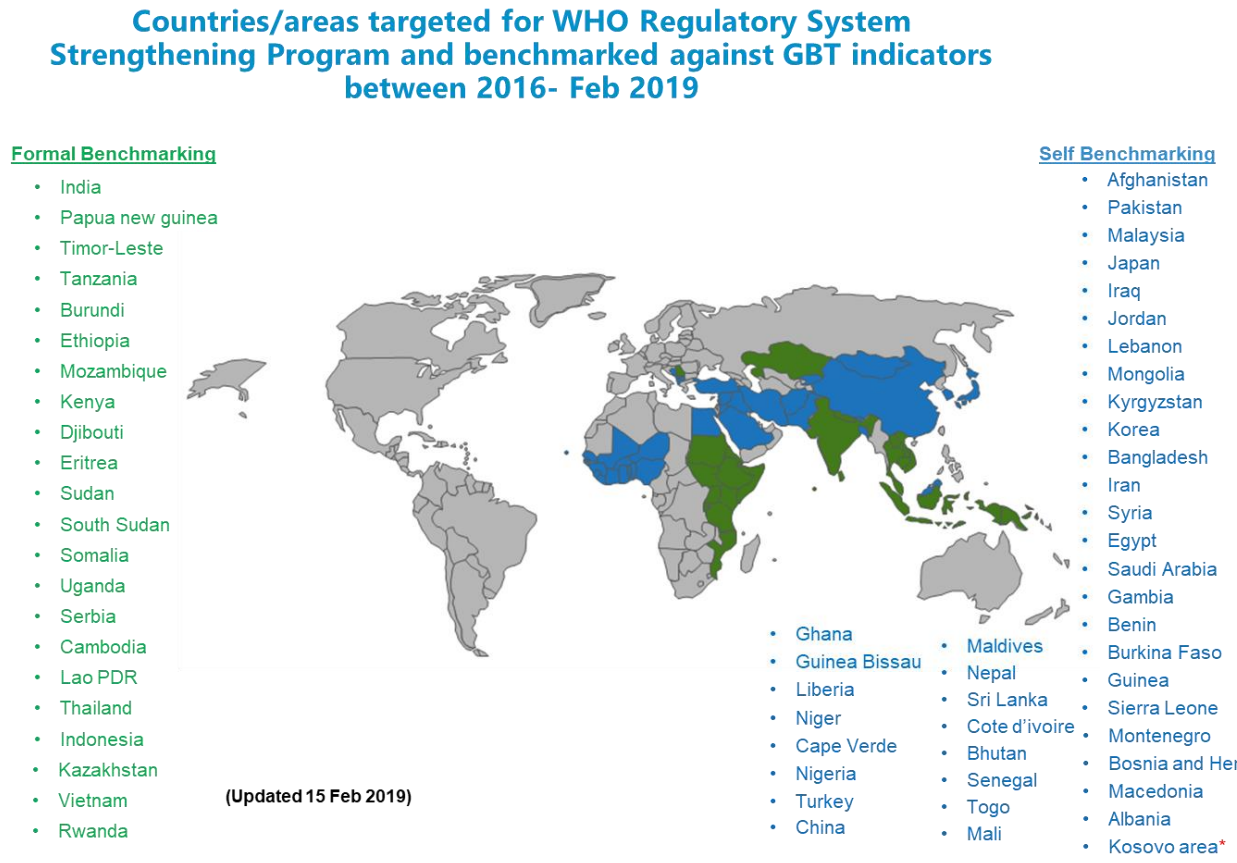
SEAR Regulatory challenges

- Country specific requirements for licensing distributors e.g.: office and staff, tender through local representative only, annual maintenance fees to continue registration
- Requirements for specifications e.g. markings, labelling color country specific and safety studies before the product is introduced in the NIPs.
- Expedited approval of PQ vaccine is not implemented for Market Authorization resulting in duplicating testing and other QC procedures despite of the PQ.
- NRA with limited capacity require registration of the product at least in 2 European countries before the product is registered.
- Sites visits of manufacturing facilities for GMP is required for MA in most of the countries despite the PQ and it is paid by the manufacturers.
- Several countries also want product testing in their NCL, which may result with increasing time for actual use from the moment the product is supplied to the country.



NRA capacity strengthening in SEA region

- Formal benchmarking in IND (2017); INO and THA (2018).
- Regional Training workshop on the use of WHO new BGT tools (2018)
- Supported self-assessment in DPRK and SRK. Formal GBT in SRK Oct 2019 and NEP Sep (2019)
- Capacity development planned endorsed by NRAs and TS is being provided in SRK (2 missions in 2018 and 1 in 2019), in DPRK with a TS for 3 months.



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x4 Levels of Maturity with specific Technical Assistance Needs

Deficiencies in most regulatory functions & high risk of high cost medicines with unassured quality.

Regulatory system in place with limited enforcement of regulatory functions high to moderate risks of high cost medicines of unassured quality

Moderate to high staff competency, specific regulatory deficiencies requiring targeted support for technical improvements to meet local pharma industry requirements

High competency staff, deficiencies that can be addressed through improved policy guidance, dialogue, and capacity building. Technical staff involved in regulatory networks, collaborative works and development of norms and guidelines

Direct Assistance

– WHO's support to include direct technical, operational and financial support to strengthen basic NRA functions focusing on QMS, licensing and PV through regional collaboration e.g.: GLO, Twining programme with strong NRA in SEA, MLQC network

Assistance through collaborative mechanisms

– WHO's support focused on filling critical regulatory gaps and reduce risks of medicines of unassured quality through promoting use of WHO PQ medicines and CIP. Regional collaboration with support for regulatory inspection, Lab access in addition to above.

Strategic Support

– WHO's support is focused and targeted to address key deficiencies and gaps in specific components of the regulatory system including full implementation of QMS and compliance with BGT

Policy Dialogue

– WHO's support is focused on advising and guiding Ministries of Health on regulatory policies and best practices including south-south exchanges and institutional capacity building. Develop formal bi-lateral collaboration to assist NRA with limited capacity

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x5 SEA Context Specific Dimensions

	Context Specific Dimensions	Example of Main Focus?
Upper MIC and LIC	Countries with limited capacity to assess product safety and quality.	Focus on basic QMS, licensing and PV and rely on products assessment conducted by strong NRA active with network and WHO initiatives including PQ products.?
Lower MIC	Countries with limited regulatory capacity and small size pharma industry supplying National programmes.	QMS across specific functions; MA, PV, Lab access and regulatory inspections. GLO and twining programme for hand-on practices?
Lower MIC	Countries with specifics regulatory deficiencies and significant pharma industry supplying local market.	Focus on deficiencies through TA to comply with all recommended regulatory functions of medicines producing country in-country training?
Upper MIC	Countries with few deficiencies producing WHO PQ products with maturity level 3.	Focus on formal BGT and monitor implementation of IDP to comply with Good regulatory Practices, collaborative mechanisms to support NRA with limited capacity substantial IT investment required?
Upper MIC	Countries with NRA maturity level 3 and above and production of PQ products.	Focus on regulatory pathways of new medicines, policy and guideline, capacity for technical collaboration, IT investment required?

Discussion points for plenary

- **What are the NRA requirements for MA in the countries importing vaccine**
- **Currently how long it takes to MA vaccines ?**
- **What are the country NRAs part or willing to join International Generic Drug Regulators Programme (IGDRP) and or apply collaborative procedures to MA vaccines ?**
- **What are the barriers to apply collaborative procedures for MA.**

Thank You