SECURE WEBINAR 18

BLUEPRINTS TO BREAKTHROUGHS:
ENHANCING VACCINE MANUFACTURING ECOSYSTEMS IN DMCS

24 OCTOBER 2024
2:00-3:30 PM Manila time

Regulatory Systems Strengthening in the Western Pacific Region

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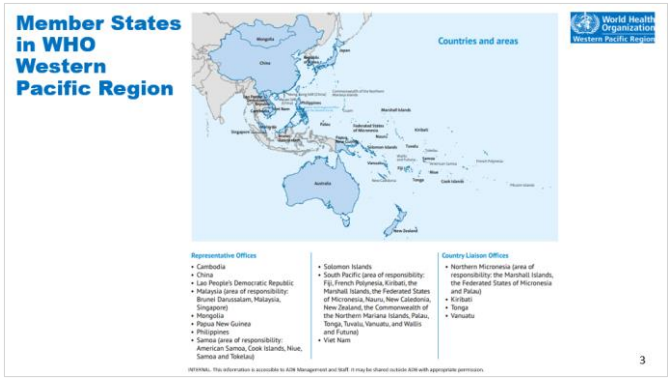
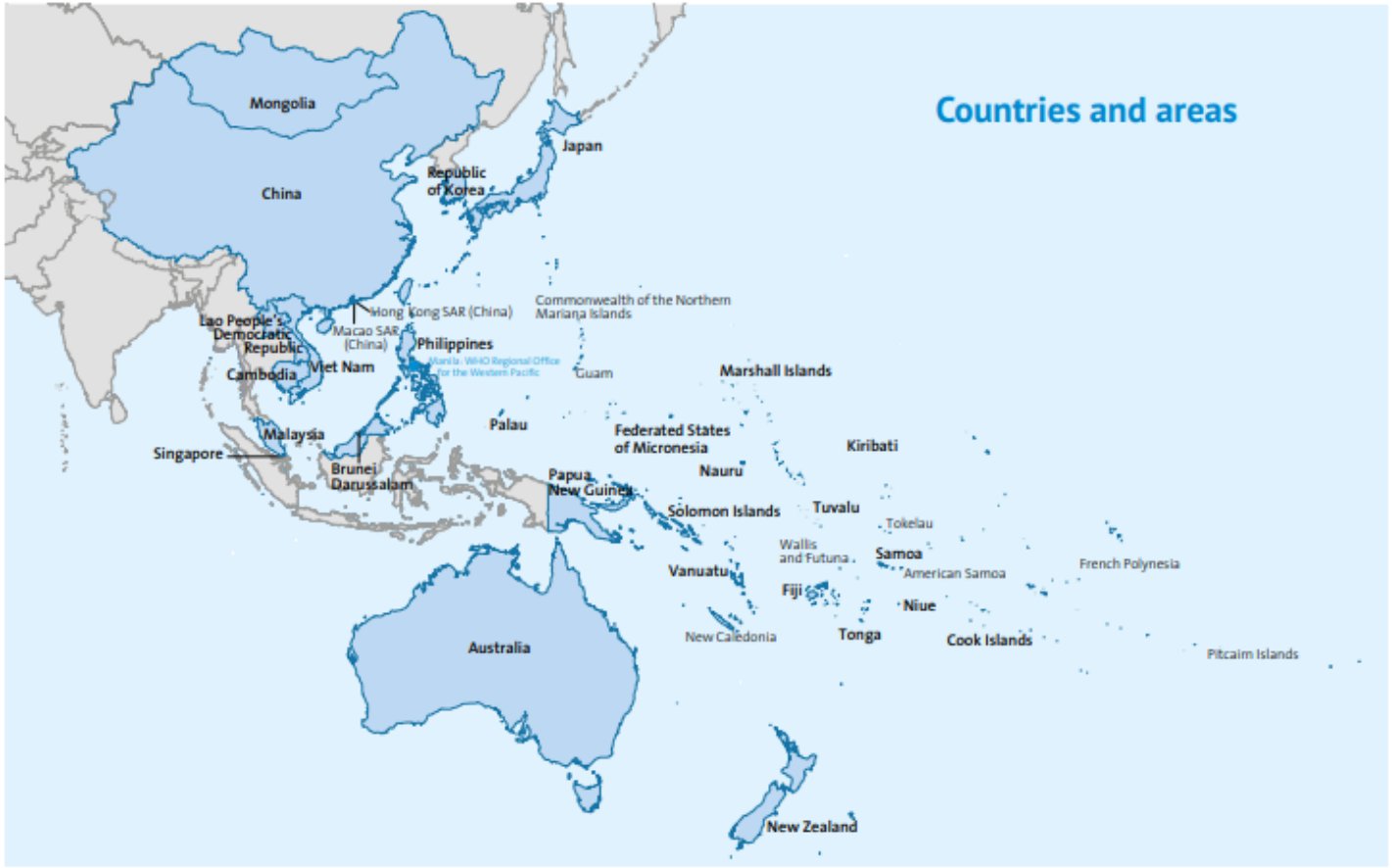
Setting the scene



Member States in WHO Western Pacific Region

World Health Organization
Western Pacific Region



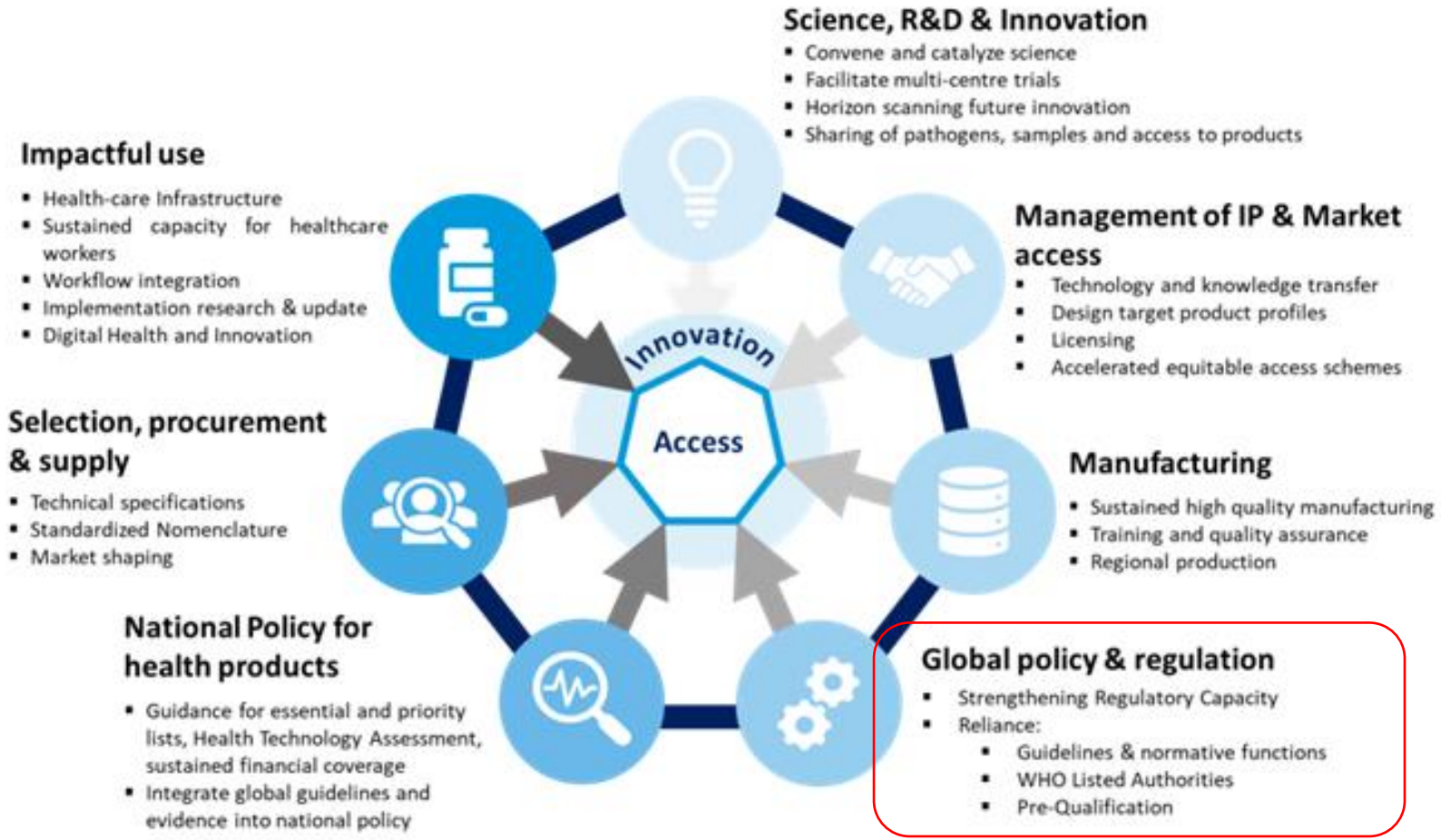
Representative Offices

- Cambodia
- China
- Lao People's Democratic Republic
- Malaysia (area of responsibility: Brunei Darussalam, Malaysia, Singapore)
- Mongolia
- Papua New Guinea
- Philippines
- Samoa (area of responsibility: American Samoa, Cook Islands, Niue, Samoa and Tokelau)
- Solomon Islands
- South Pacific (area of responsibility: Fiji, French Polynesia, Kiribati, the Marshall Islands, the Federated States of Micronesia, Nauru, New Caledonia, New Zealand, the Commonwealth of the Northern Mariana Islands, Palau, Tonga, Tuvalu, Vanuatu, and Wallis and Futuna)
- Viet Nam

Country Liaison Offices

- Northern Micronesia (area of responsibility: the Marshall Islands, the Federated States of Micronesia and Palau)
- Kiribati
- Tonga
- Vanuatu

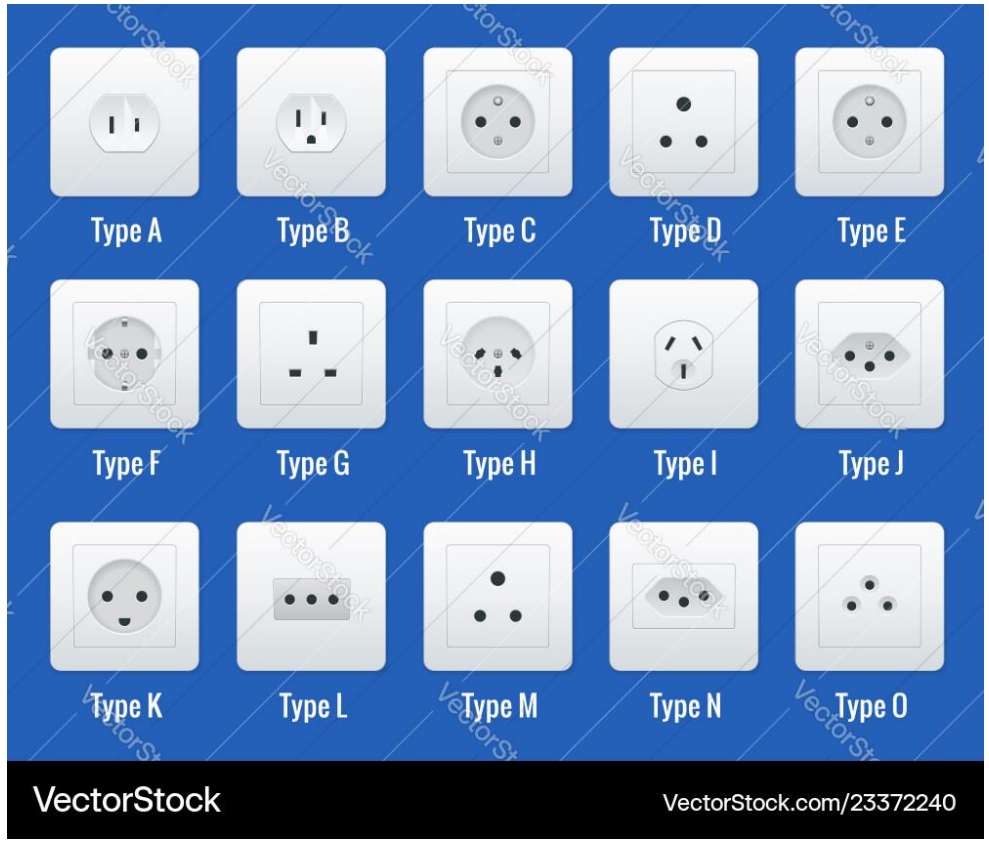
WHO ecosystem approach to accelerating access to life-saving innovation



All for Health, Health for All: investment case 2025–2028 (who.int))

Why do we need to use a unified global standard for Medical Products?

Travel nightmare



To Protect People from Diseases without Barriers

Making travelers happier

What are the key functions of the NRA

National Regulatory Authority: Structure and Role

A regulatory authority is a public institution(s) or governmental body or bodies authorized by law to exercise independent regulatory oversight over the development, production, marketing and surveillance of medical products.

NRAs are often structured as

- Centralized,
- Decentralized,
- Discrete

The regulatory authority plays a critical role in:

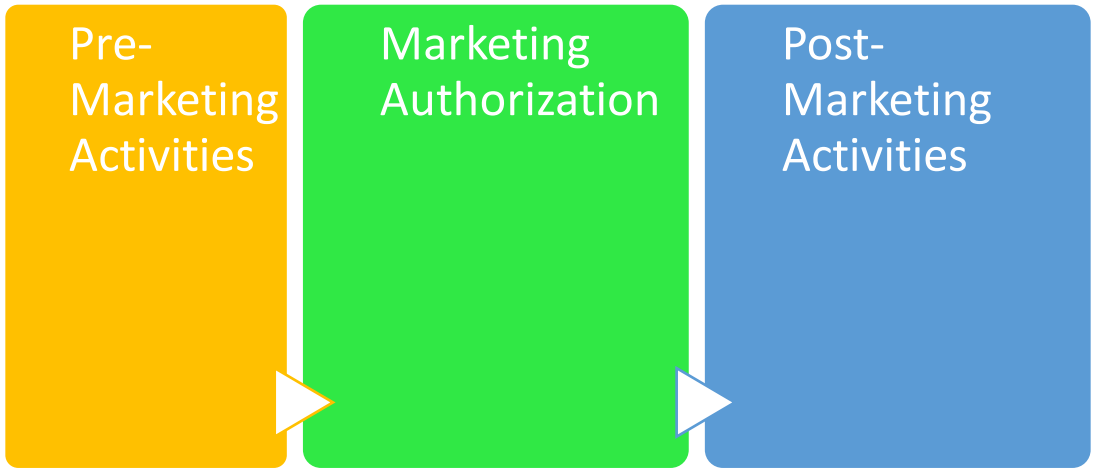
(a) ensuring the quality, safety, efficacy/ performance of medical products,

(b) overseeing the supply chain in which their quality is ensured until they reach the patient/consumer and

(c) ensuring the relevance and accuracy of product information.

What are the critical product attributes of vaccines, medicines, and medical devices including in-vitro diagnostics ('medical products')?

- Safety and Efficacy (Performance for MeDev): tested in the pre-market period
- Quality: must be traceable to those of the clinical lots and be met consistently
- Safety and Effectiveness (Performance for MeDev) are monitored and updated continuously in the post-market period



WHO RSS program launched in 1997 with a new statement of "a Vaccine of Known Good Quality", that adopts systems approach to NRA strengthening

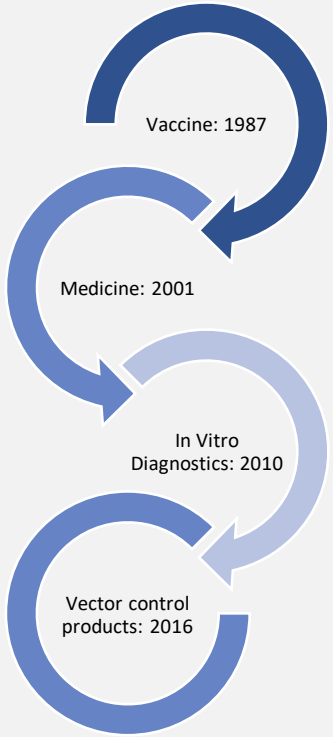
WHO Vaccine Policy Statement*

- ☑ the NRA independently controls the quality of the vaccine in accordance with the six specified functions defined by WHO
- ☑ there are no unresolved confirmed reports of quality-related problems

6 Critical Functions of NRA

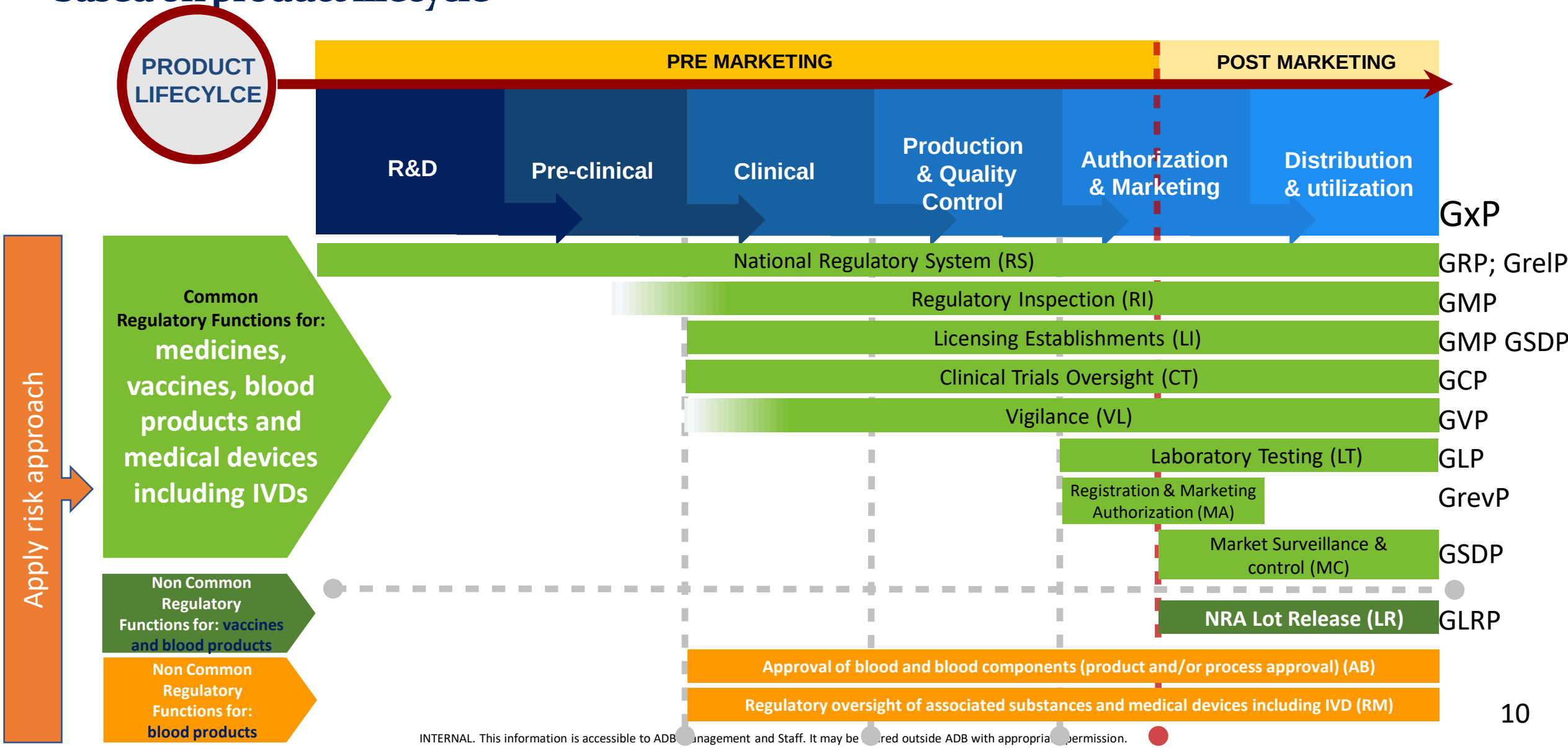
- **A** published set of requirements for licensing
- **S**urveillance of vaccine field performance
- **S**ystem of lot release
- **U**se of laboratory when needed
- **R**egular inspections for Good Manufacturing Practice (GMP) compliance
- **E**valuation of clinical performance

WHO Prequalification Timeline by Products

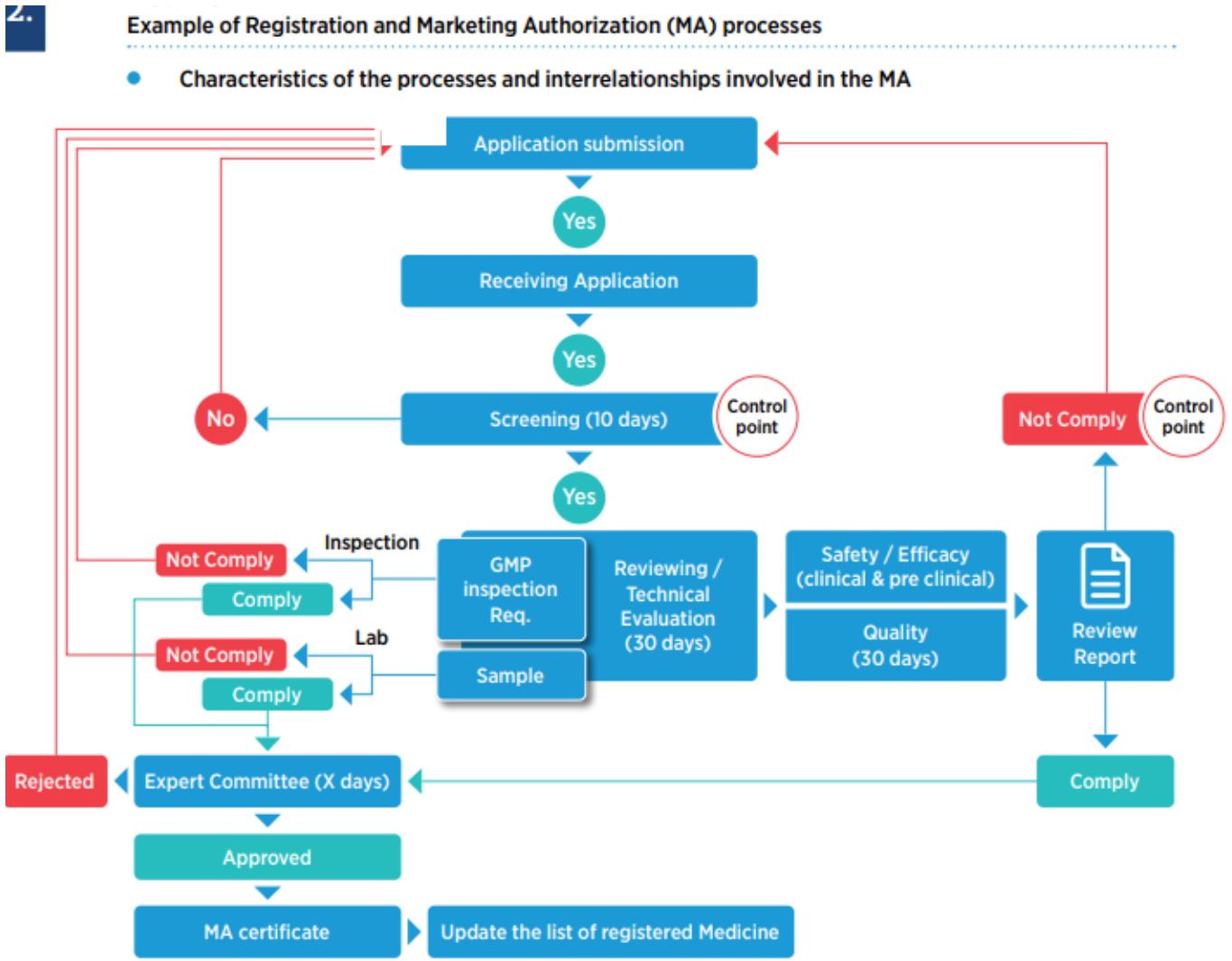


* WHO GPV (Global Programme for Vaccines and Immunization) Policy statement 1997: source;
** WHO GPV Policy on 6 critical functions of NRA: source

WHO recommended regulatory functions for medicines, vaccines, blood products and medical devices including IVDs based on product lifecycle

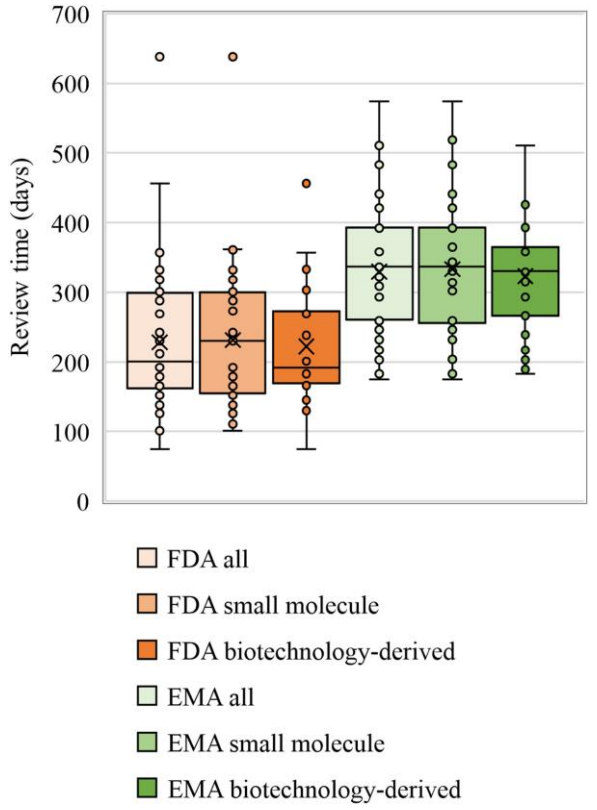


Example of Registration and Marketing Authorization (MA) process



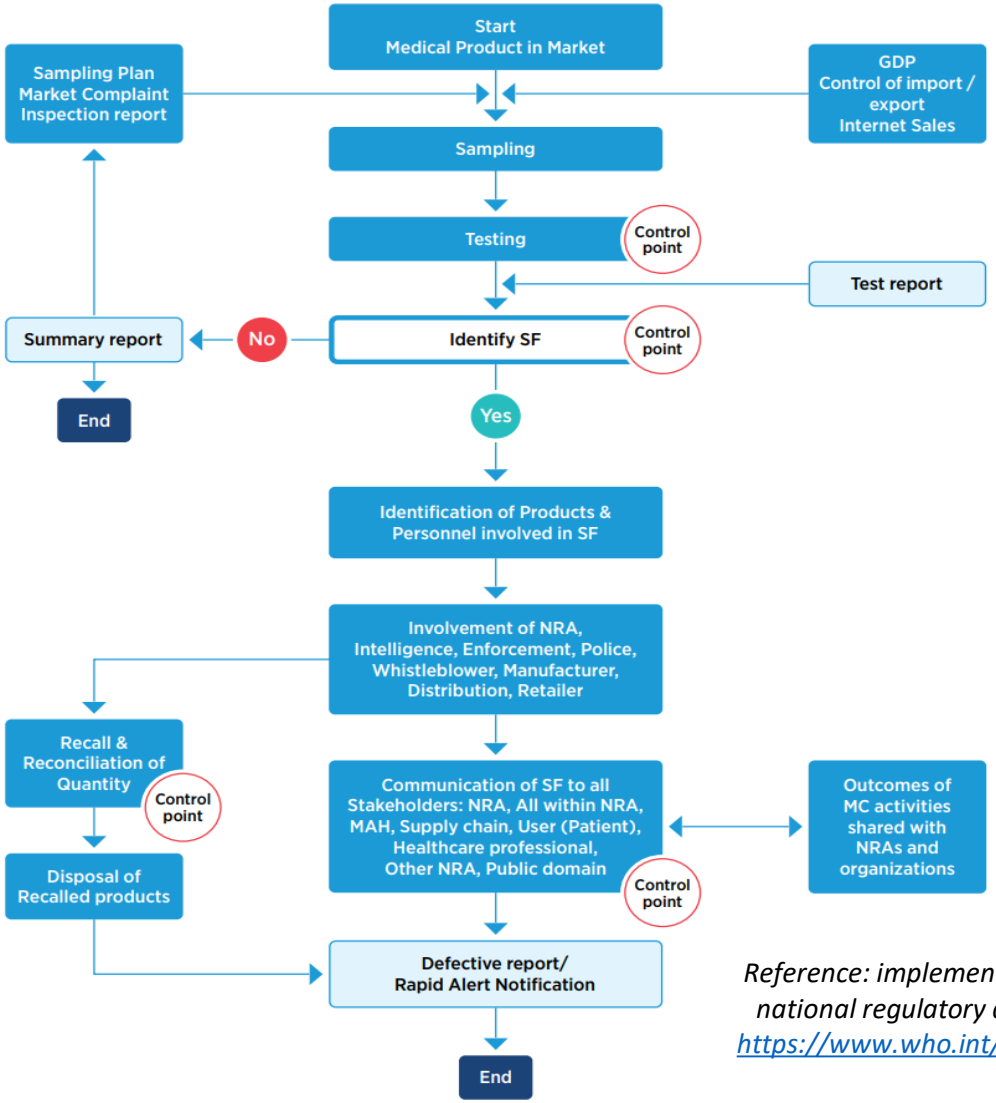
Reference: implementing quality management systems in national regulatory authorities: Examples and practices https://www.who.int/publications/i/item/9789240022379

A detailed analysis of expedited regulatory review time of marketing authorization applications for new anticancer drugs in the US and EU

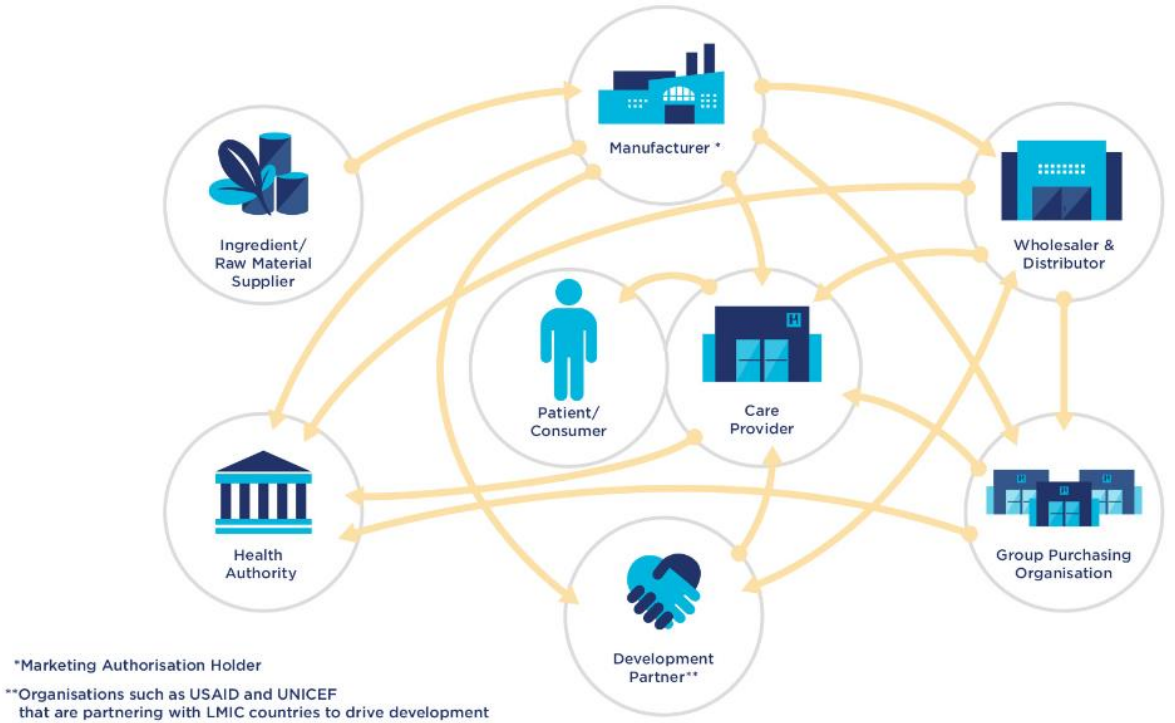


Clinical Translational Sci, Volume: 15, Issue: 8, Pages: 1959-1967, First published: 13 May 2022, DOI: (10.1111/cts.13308)

Example of Marketing Surveillance and Control (MC) process



GS1 Standards and Traceability in Healthcare



*Marketing Authorisation Holder

**Organisations such as USAID and UNICEF that are partnering with LMIC countries to drive development

Product Identifier:

Expiry Date:

Batch Number:

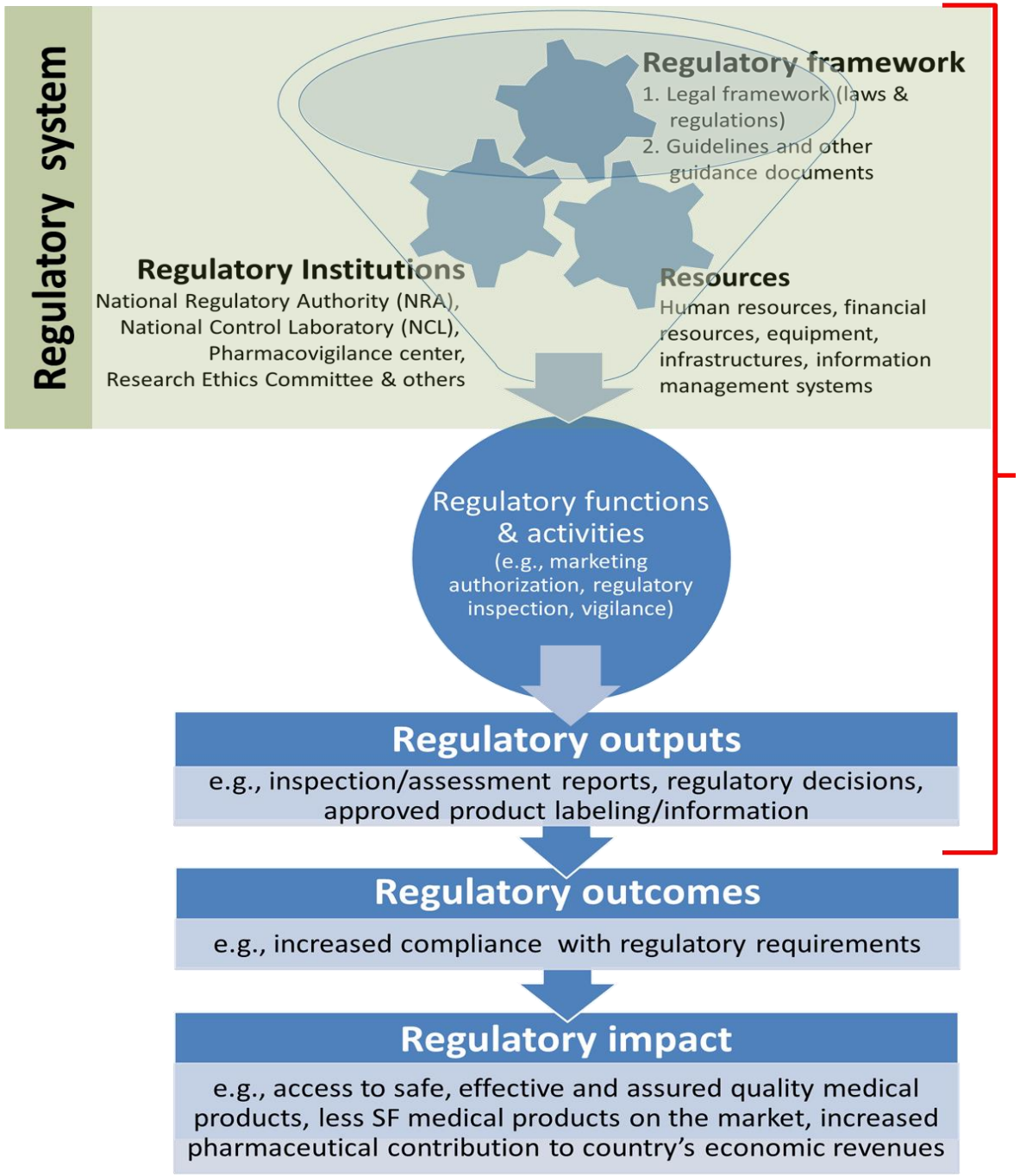
Serial Number:

Reference: implementing quality management systems in national regulatory authorities: Examples and practices
https://www.who.int/publications/i/item/9789240022379

GS1 Healthcare Strategy 2023-2027 | GS1

What outcomes and impact does the NRS want to achieve

General concept of regulatory system



According to Good regulatory practice principals and enablers

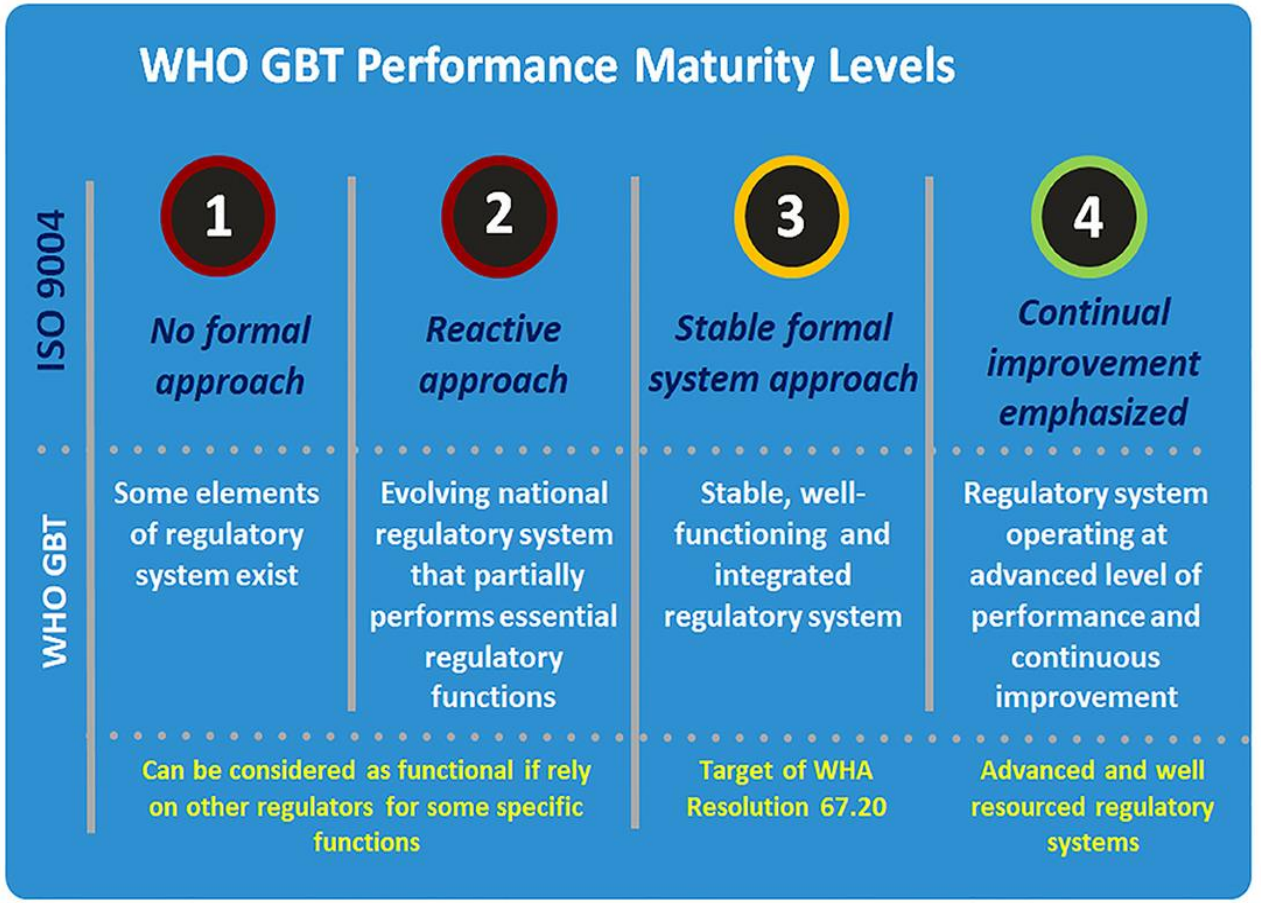
Source: Good regulatory practices in the regulation of medical products 9789240020900-eng.pdf (who.int)

What are these terms: Benchmarking and WLA

Global Benchmarking Tools (GBT) and concept of maturity level (ML)

GBT is a tool to objectively evaluate the regulatory system:

- ✓ ***Medicines and vaccines using GBT***
- ✓ ***Blood products*** *(including whole blood, blood component and plasma-derived products) using* ***GBT + blood***
- ✓ ***Medical devices*** *(including in vitro diagnostics) using* ***GBT + medical devices, under revision***



- ✓ ***ML3 for vaccine regulation*** ***is an eligibility criterion for a manufacturer to apply for WHO prequalification that is intended to supply to the UN market***

‘WHO Listed Authority’ replacing ‘Stringent Regulatory Authority’

A WHO Listed Authority (WLA) is a regulatory authority or a regional regulatory system which has been documented to comply with all the relevant indicators and requirements specified by WHO for the requested scope of listing based on an

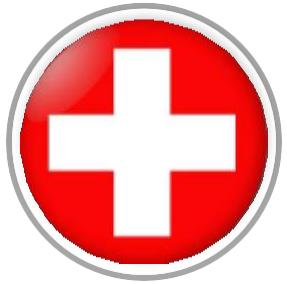
An established benchmarking (GBT) + a **Performance Evaluation (PE) process**

https://www.who.int/publications/i/item/9789240023444

First three WLAs

31st October 2023

SRA



Switzerland

Swissmedic

tWLA

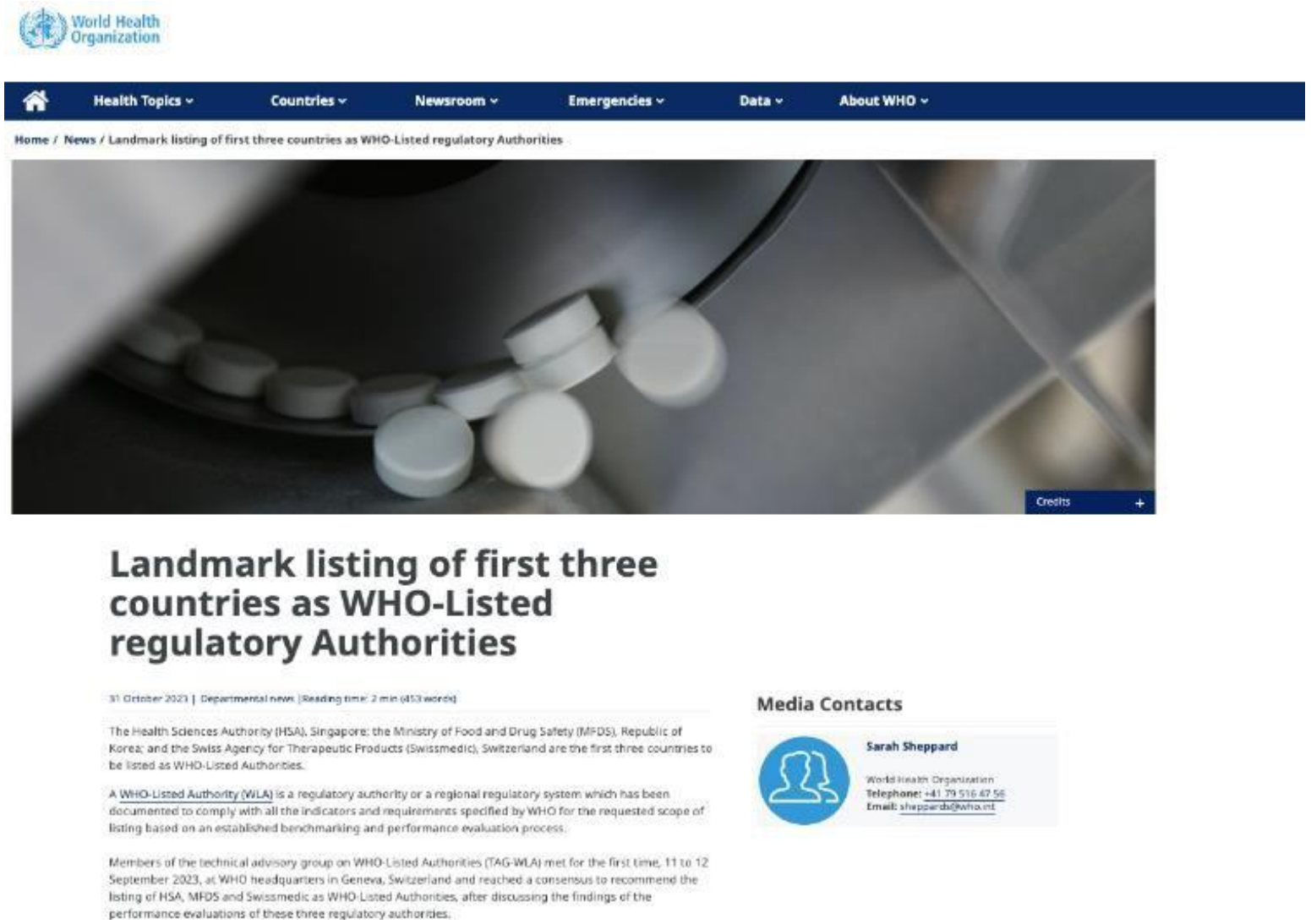
Republic of Korea

MFDS

ML4 NRA

Singapore

HSA



https://www.who.int/news/item/31-10-2023-landmark-listing-of-first-three-countries-as-who-listed-regulatory-authorities

33 new WLAs

20th May 2024

RRS

European Medicines Regulatory Network

EC/EMA

+30 NCAs

SRA

United States of America

US FDA

ML4 NRA

Singapore

HSA*

* MC function

https://www.who.int/news/item/20-05-2024-largest-number-of-regulatory-agencies-for-medical-products-approved-as-who-listed-authorities

Total WLA: 36 Regulatory Authorities and 34 Member States

Is there a Regional Cooperation & Collaboration Mechanism among NRAs and Partners?

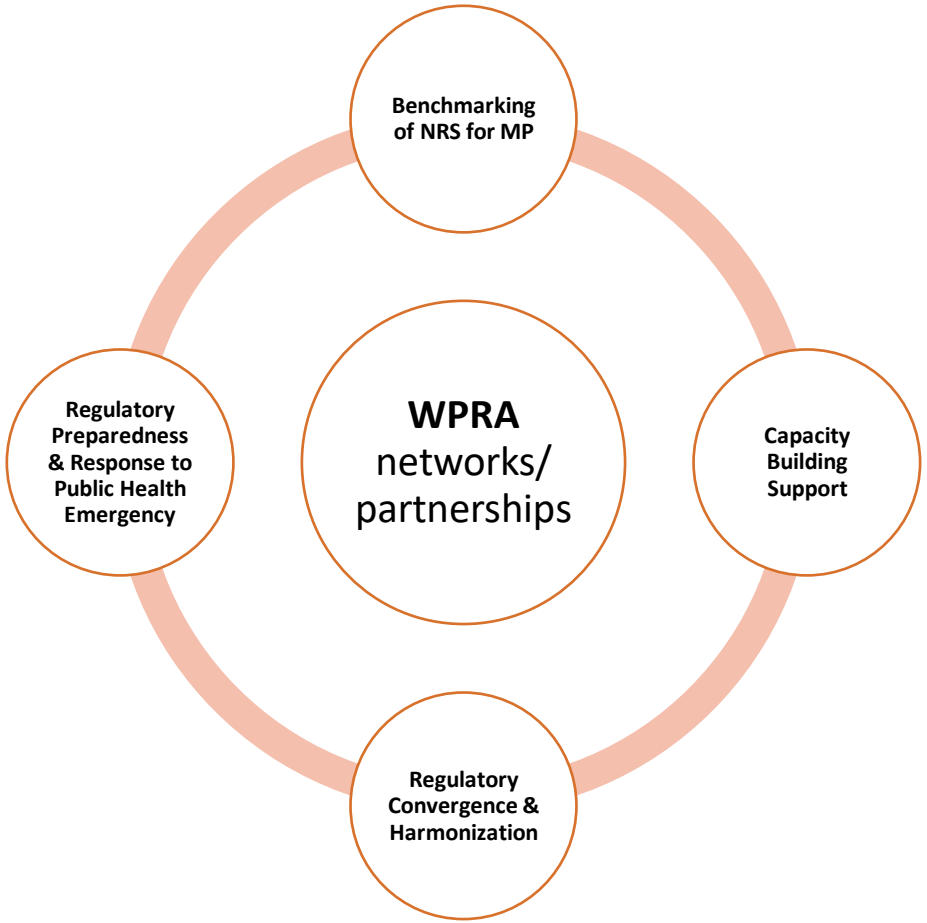
Medicine & Vaccine Production, National Control Laboratories in the Western Pacific

World Health Organization
Western Pacific Region

Countries	Medicine Production	Vaccine Production	Medicine NCL	Vaccine NCL	Vaccine Lot Release System	Risk-based LR
Australia	Yes	Yes	Yes	Yes	Yes	Yes
Brunei Darussalam	Yes		Yes			
Cambodia	Yes		Yes			
China	Yes	Yes	Yes	Yes	Yes	Yes
Japan	Yes	Yes	Yes	Yes	Yes	Yes
Lao PDR	Yes		Yes			
Malaysia	Yes	Yes	Yes	Developing	Yes	Yes
Mongolia	Yes		Yes			
New Zealand	Yes		Yes			
Papua New Guinea	Yes		Yes			
Philippines	Yes		Yes	Developing	YES (SLP review)	
Republic of Korea	Yes	Yes	Yes	Yes	Yes	Yes
Singapore	Yes		Yes			
Viet Nam	Yes	Yes	Yes	Yes	Yes	
Pacific Island Countries	Medical Oxygen*			No	No	

- All countries listed above have established national medicines control laboratories (except the Pacific Island Countries), as of Oct 2024
- New Zealand: Has National Medicine QA Laboratory, no vaccine laboratory but has an agreement with TGA for vaccine quality testing
- Philippines and Malaysia: Existence of legal and regulatory provisions for lot release.

Harnessing Regulatory System Strengthening, Cooperation, Convergence and Harmonization through Western Pacific Regional Alliance of NRAs for Medical Products (WPRA)



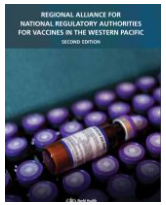
Regulatory Cooperation/Collaboration through WPRA

2011
- 1st Workshop, Korea

2012
- 1st Taskforce meeting, Australia

2013
- 2nd Workshop
- 2nd Taskforce meeting
- 1st edition of concept paper
- 1st meeting of Steering Committee

2014



- 3rd Workshop
- 2nd edition of Concept paper, WPRO

2015
- 4th Worksh op, Korea

2016
- 5th Workshop, WPRO
- Expansion to include medicines Formation of taskforce review group for the 3rd Ed Concept Paper, WPRO

2017

- 6th Workshop, WPRO
- Endorsement of Regional Action Framework Agenda
- Development of the terms of reference of the Alliance

2018
- 7th Workshop, Philippines
- Renewal of Steering Committee Membership, WPRO

2019
- 8th Workshop, Japan

2020
- Monthly virtual meeting organized in response to regulatory issues during COVID-19 pandemic

2021
- 10th meeting- virtual meeting on regulatory preparedness during public health emergencies

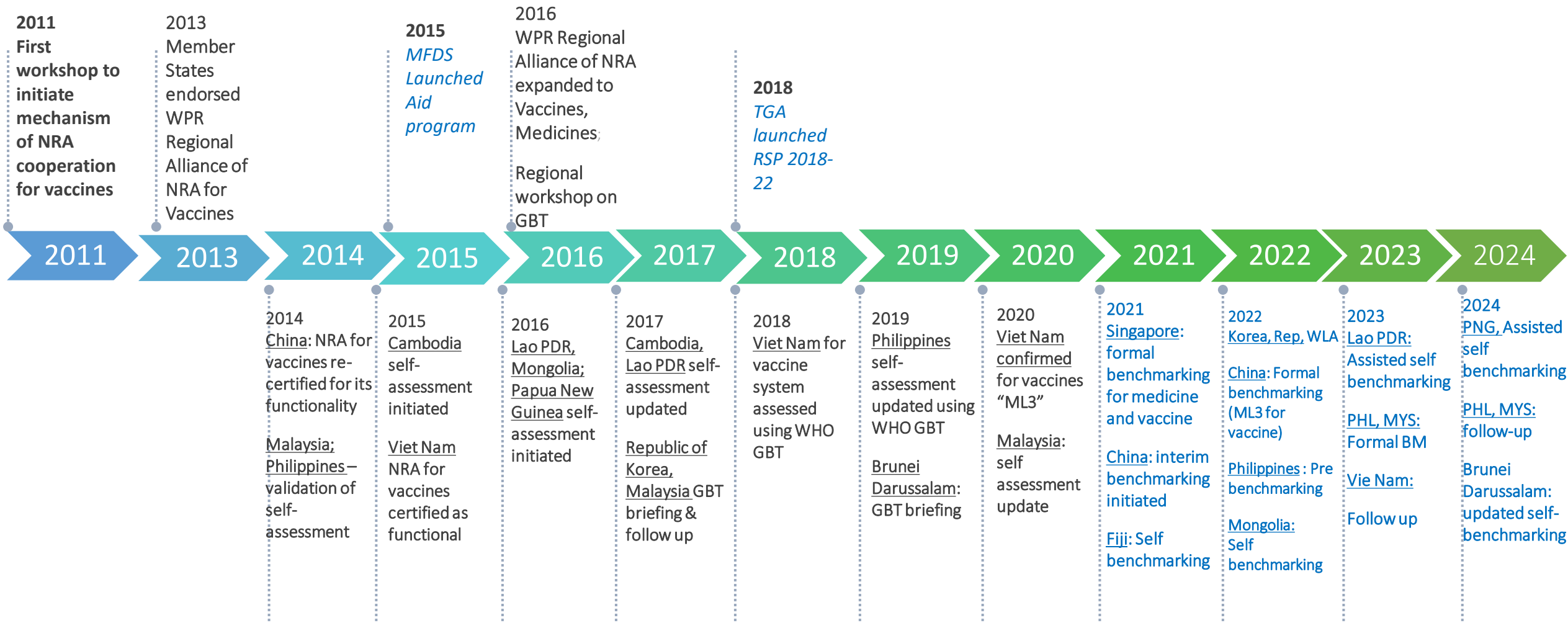
2022
- 11th meeting – regulatory transition

2023
- 12th meeting – ePharmacy, medical errors, SF

2024
- 13th meeting – emerging economies, small states, SF MP

Key milestones of NRS benchmarking in WHO Western Pacific Region

World Health Organization
Western Pacific Region

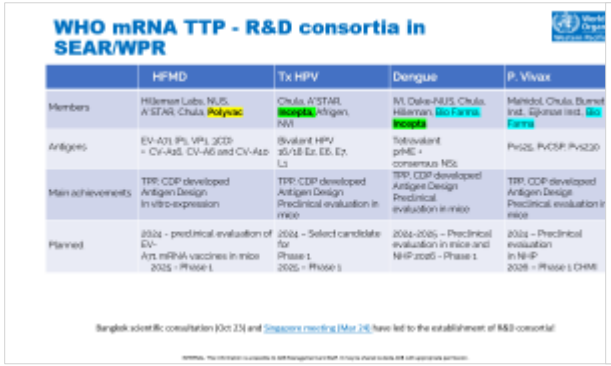


Achievements of regulatory systems in the Western Pacific

Republic of Korea and Singapore:	• Achieved WLA status in 2023-2024; **Rep of Korea** – Vaccines & Medicines; **Singapore** - Medicines
Viet Nam and China:	• Maintained ML3 for **vaccine** regulation after re-benchmarking in 2018 and 2022, respectively
Philippines and Malaysia:	• Hosted formal WHO benchmarking in 2023: **Philippine** – Medicines; **Malaysia** – Vaccines and Medicines
Brunei Darussalam, Fiji, Mongolia, Lao PDR, Papua New Guinea:	• Accomplished self-benchmarking; **Scope** - Medicines
Australia, Japan:	• Transitioning from SRA to WLA: The evaluation process ongoing for both Vaccines and Medicines

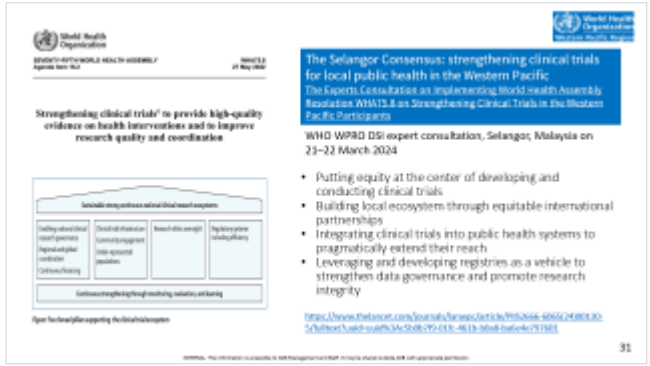
What are the current efforts to close equity gaps in improving access to vaccines through local production in low-resource settings

mRNA TTP



GTH-B

CT ecosystem



WHO mRNA TTP - R&D consortia in SEAR/WPR

	HFMD	Tx HPV	Dengue	P. Vivax
Members	Hilleman Labs, NUS, A*STAR, Chula, **Polyvac**	Chula, A*STAR, **Incepta,** Afrigen, NVI	IVI, Duke-NUS, Chula, Hilleman, Bio Farma, **Incepta**	Mahidol, Chula, Burnet Inst., Eijkman Inst., Bio Farma
Antigens	EV-A71 (P1, VP1, 3CD) + CV-A16, CV-A6 and CV-A10	Bivalent HPV 16/18 E2, E6, E7, L1	Tetravalent prME + consensus NS1	Pvs25, PvCSP, Pvs230
Main achievements	TPP, CDP developed Antigen Design In vitro expression	TPP, CDP developed Antigen Design Preclinical evaluation in mice	TPP, CDP developed Antigen Design Preclinical evaluation in mice	TPP, CDP developed Antigen Design Preclinical evaluation in mice
Planned	2024 - preclinical evaluation of EV-A71 mRNA vaccines in mice 2025 - Phase 1	2024 – Select candidate for Phase 1 2025 – Phase 1	2024-2025 – Preclinical evaluation in mice and NHP 2026 - Phase 1	2024 – Preclinical evaluation in NHP 2026 – Phase 1 CHMI

Bangkok scientific consultation (Oct 23) and Singapore meeting (Mar 24) have led to the establishment of R&D consortia!

Challenges in Regulatory Oversight of mRNA Vaccine Local Production in Bangladesh and Viet Nam

World Health Organization
Western Pacific Region

- Developing guidelines for clinical trials
- Developing guidelines for chemistry, manufacturing and control (CMC), nonclinical and clinical evaluation
- Establishing independent quality control testing
- Post-market surveillance and pharmacovigilance
- Regulatory oversight of good manufacturing practices
- Aligning local regulatory standards with international guidelines

Source: WHO. A case study on the ecosystem for local production of pharmaceuticals, vaccines and biologicals: The Bangladesh context https://iris.who.int/bitstream/handle/10665/376686/9789240092808-eng.pdf?sequence=1

WHO Global Training Hub for Biomanufacturing (GTH-B)

IVI
Participants during the 2022 Introductory Course for Biologics Development and Manufacturing
Credits

WHO
Dr Yukiko Nakatani, WHO ADG, Access to Medicines and Health Products (left) and Mr Hwang Seunghyun Director General, Global Vaccine Hub Office at the MoH and Welfare from Republic of Korea (right) at the biomanufacturing training signing ceremony
Credits

Credit: MOHW, Republic of Korea

World Health Organization

SEVENTY-FIFTH WORLD HEALTH ASSEMBLY
Agenda item 16.2

WHA75.8
27 May 2022

Strengthening clinical trials[1] to provide high-quality evidence on health interventions and to improve research quality and coordination

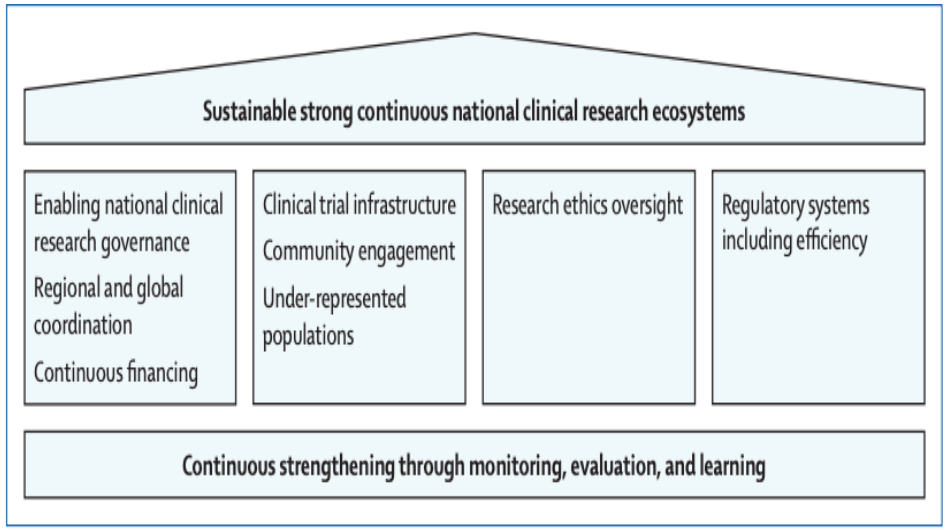


Figure: Four broad pillars supporting the clinical trial ecosystem

World Health Organization
Western Pacific Region

The Selangor Consensus: strengthening clinical trials for local public health in the Western Pacific

The Experts Consultation on Implementing World Health Assembly Resolution WHA75.8 on Strengthening Clinical Trials in the Western Pacific Participants

WHO WPRO DSI expert consultation, Selangor, Malaysia on 21–22 March 2024

- Putting equity at the center of developing and conducting clinical trials
- Building local ecosystem through equitable international partnerships
- Integrating clinical trials into public health systems to pragmatically extend their reach
- Leveraging and developing registries as a vehicle to strengthen data governance and promote research integrity

https://www.thelancet.com/journals/lanwpc/article/PIIS2666-6065(24)00130-5/fulltext?uuid=uuid%3Ac5b0b7f9-01fc-461b-b0a8-ba6e4e797601

Key takeaways

- Strengthening regulatory systems for medicines, vaccines, and medical devices including in vitro diagnostics ensures that these products are safe, effective, and of assured quality.
- Strengthening regulatory systems also promotes innovation, and ensures regulatory predictability with enhanced transparency, making vaccines and other medical products more accessible and affordable.
- By aligning with global standards, it also builds trust in health systems and facilitates global cooperation in product distribution.
- Efforts to close equity gaps in access to medical products in low-resource settings focus on local production through technology transfer and capacity building, like the WHO's mRNA vaccine hub, WHO Global Training Hub for Biomanufacturing, and strengthening clinical trials.
- Moving forward, partnerships between governments, international organizations, and the private sector will ensure resources, technical support, and infrastructure to boost local manufacturing and appropriate oversight by competent regulatory authorities to ensure quality.

SECURE WEBINAR 18

BLUEPRINTS TO BREAKTHROUGHS: ENHANCING VACCINE MANUFACTURING ECOSYSTEMS IN DMCS

24 OCTOBER 2024
2:00-3:30 PM Manila time

Vaccines save lives