Working together to build Effective and efficient regulatory systems

From pandemic response into supporting global regulatory strengthening, a critical role to provide affordable access to quality-assured medical products

USP - Regulatory Best Practices for Global Access to Medicines, Including Anti-TB Medicines (August 16th 2022)

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Access to Medicines and Health Products (MHP)

ADG - Mariângela Simão

Health Products Policy and Standard (HPS)
Clive Ondari

Regulation and Prequalification (RPQ)
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- IVD Assessment — **Irena Prat**
- Medicines Assessment — **Matthias Stahl**
- Vaccines & Immunization Devices Assessment — **Carmen Rodriguez**
- Vector Control Products Assessment — **Marion Law**
- Medical Devices — **TBD**

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- Facilitated Product Introduction — **Samvel Azatyan*&****
- Laboratory Network and Services — **Gaby Vercauteren**
- Pharmacovigilance — **Shanthi Pal**
- Incidents and SF Medical Products — **Rutendo Kuwana**

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Jicui Dong

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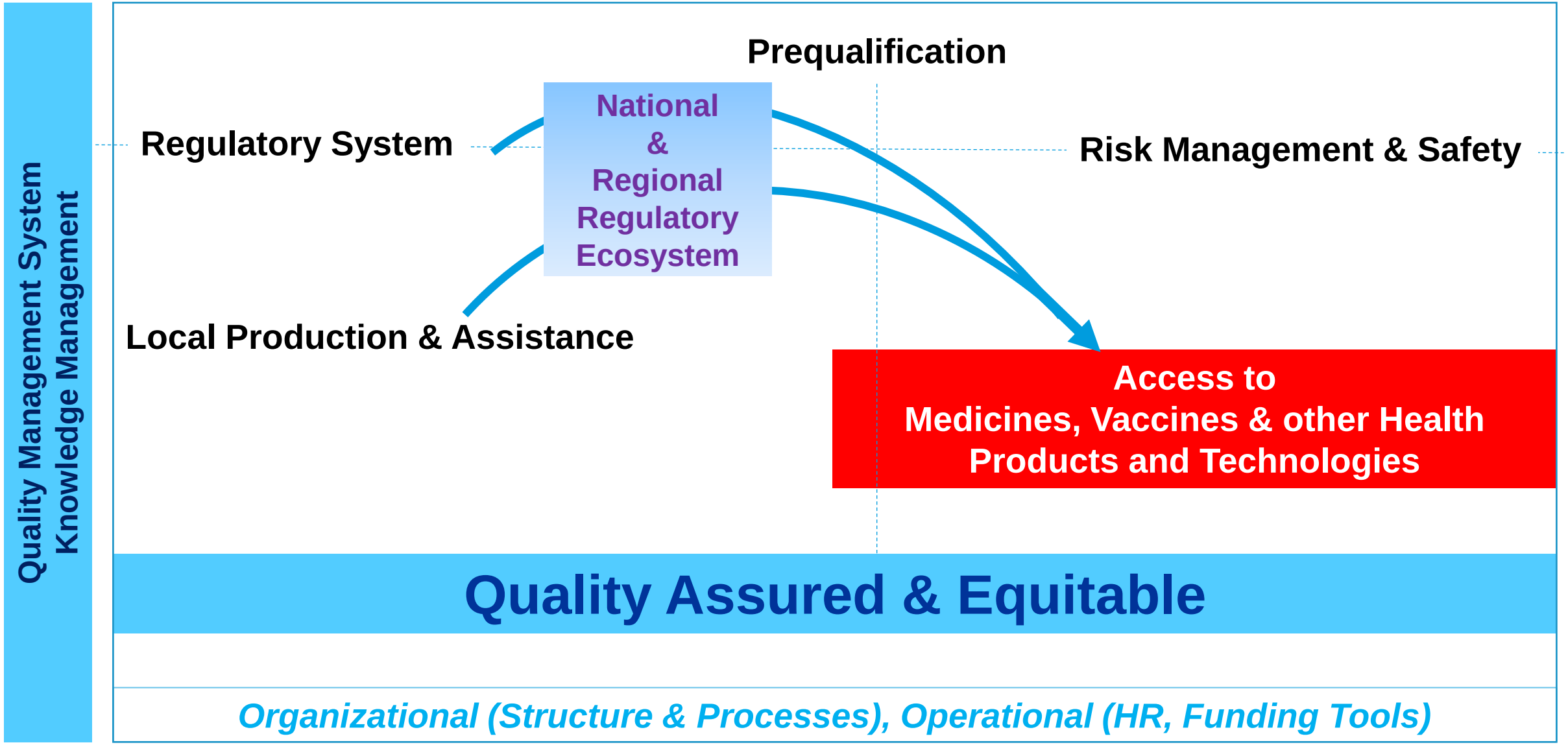
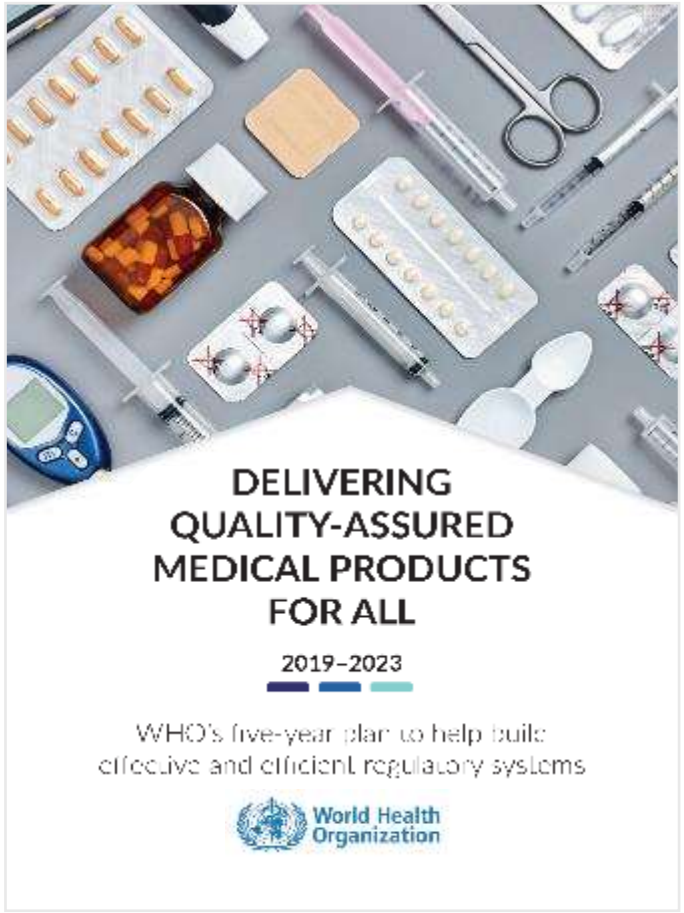
- Quality Management Systems** — **(Jan-Anton Norder)**
- Knowledge Management**

* acting
** under recruitment

Regulation and Prequalification (RPQ)



WHO's Regulatory Strategic Priorities: 2019-2023



1. Strengthen country and regional regulatory systems
2. Improve regulatory preparedness for public health emergencies
3. Reinforce and expand WHO prequalification & product risk assessment
4. Increase the impact of WHO regulatory support activities

These strategic guide WHO regulatory activities

- ✓ Benchmarking and technical assistance to address regulatory gaps
- ✓ Promoting regulatory convergence, harmonization, work-sharing and reliance mechanisms
- ✓ Improving countries' ability to carry out risk-based post-marketing surveillance to securing supply chains against SF products
  - Includes strengthening national quality laboratories
- ✓ Broaden the prequalification programme
- ✓ Leverage political attention and commitment to advance accountability
- ✓ Promote and support sustainable and quality-assured local production through technical assistance

https://www.who.int/medicines/news/2019/strong-reg-systems-to-reach-UHC/en/

A reminder: WHO Regulatory Activities

Ensuring normative and technical excellence drives impact at country level

Technical Standards & Specifications

- Set global norms and standards (written & physical) and nomenclatures
- Increase common understanding on regulatory requirements by authority & manufacturer
- Standardize approach used by quality control labs

Prequalification

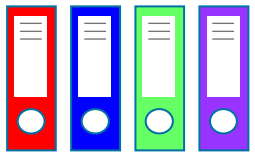
- Assure safety, quality efficacy & appropriateness of medical products used in LMICs, including medicines, vaccines, medical devices, cold chain equipment, vector control products & in vitro diagnostics
- Increase competition to shape the market

Regulation & Safety

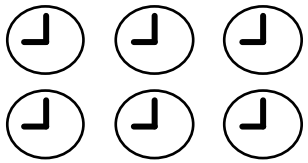
- Strengthen regulatory systems in countries and regions
- Promote regulatory cooperation, convergence and transparency through networking, work-sharing and reliance
- Mitigate risks and protect against substandard / falsified products

Local production & assistance

- Provide holistic & coordinated support to strengthen local production and technology transfer
- including
  - guidance tools, situational analyses for sustainable quality local production
  - strengthening local production, capacity building and specialized technical assistance



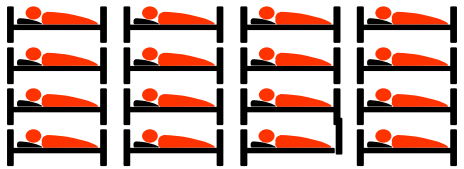
Decreased regulatory burden



Reduced time for regulation

Increased regulatory capacity in LMIC

Decreased cost of regulation



Reduced mortality and morbidity

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World Health Organization

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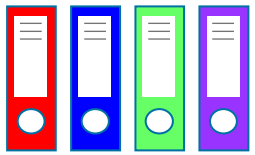

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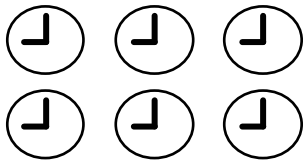

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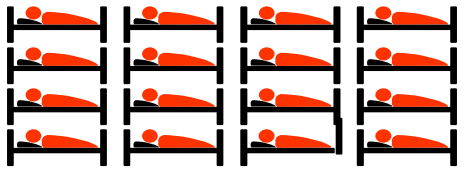
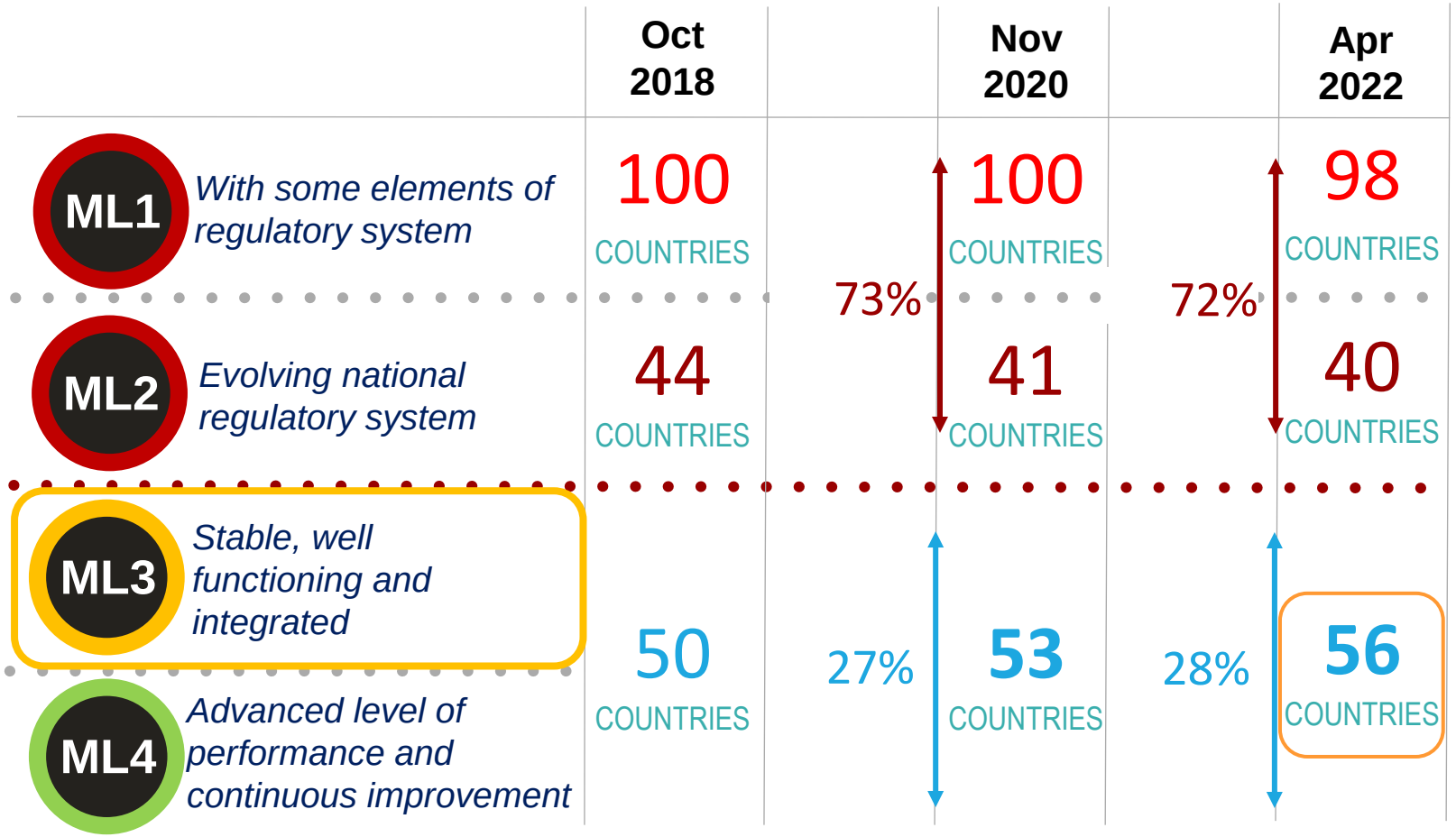


Reduced mortality and morbidity

Global status of national regulatory systems, April 2022

World Health Organization



Vaccines developed in countries with weak regulatory systems, i.e., ML1/ML2, are not eligible for EUL or prequalification

[Singapore medicines regulator world's first to achieve the highest maturity level (ML4) following assessment] (28 Feb 2022)

ML3 **GOAL of WHA Resolution 67.20**

ML: *(regulatory system) maturity level*

Nigeria and Egypt announced as ML 3 in March 2022

Timeline of events: ICMRA, COVAX RAG and R&D Blueprint

World Health Organization

Unite, Collaborate & Cooperate

April 2020 initiation of ACT-Accelerator

11 Mar 2020
WHO pandemic declaration

22 Jun 2020 ICMRA workshop
- Position on Ph3 Vx trials
- Data requirements for Ph3 Vx trials

18 Mar 2020 ICMRA workshop
Data requirements for Ph1 Vx trials

06 Nov 2020 WHO-ICMRA Joint statement
Improved regulatory alignment on COVID-19 medicines and vaccines

Technical brief: COVAX RAG
Synopsis from Aug – Oct 2020 COVAX RAG meetings

10 Feb 2021 ICMRA workshop
COVID-19 Virus Variants

13 Jan 2021 ICMRA workshop
Vx safety collaboration

24 Jun 2021 ICMRA workshop
COVID-19 Virus Variants

12 Jan 2022 ICMRA workshop
Omicron variants

7-8 July 2021 ICMRA workshop
Enabling manufacturing capacity in the COVID-19 pandemic

01-02 Dec 2021 ICMRA Summit
Global public health emergencies and regulatory systems – moving forward

07 May 2021 WHO-ICMRA Joint statement
Transparency and data integrity

11 Jun 2021 WHO-ICMRA Joint statement
How COVID-19 vaccines are regulated for safety and effectiveness

Technical brief: COVAX RAG
Synopsis from Apr 2021 COVAX RAG meeting

Technical brief: COVAX RAG
Synopsis from May 2021 COVAX RAG meeting

03 Dec 2021 ICMRA Report
Review of regulatory flexibilities/agilities as implemented by NRAs during pandemic

2020 Feb Apr Dec 2021 Jan Feb Mar Apr May Jun Aug Nov Dec 2022 Jan Feb

29 Apr WHO Vx TPP

17 Apr ToR WHO WG on Vx TPP

07 Dec 2020
Human challenge model

12 Jan 2021
New variants: Knowledge gaps & research

11 Feb 2021
Methodological Approaches to assess variants effect on Vx Efficacy, Effectiveness and Impact

26 May 2021
COVID-19 Vx Correlates of protection

13-14 May 2021
COVID-19 Global Research & Innovation Forum

23 Feb 2022
Developing a framework for evaluating new COVID-19 vaccines

14 Feb 2022
What recent evidence do we have that omicron is evading immunity and what are the implications?

28 Jan 2022
Why do we need a pan-sarbecovirus Vx?

29 Mar 2021 1st Global consultation
Assessing the Impact of SARS-CoV-2 VoC on Public Health Interventions

10 Jun 2021 2nd Global consultation
Assessing the Impact of SARS-CoV-2 VoC on Public Health Interventions

15 Dec 2021
Evidence & implications: omicron is evading immunity

05 Feb 2020 SARS Vx candidates

11-12 Feb 2020
Global Research & Innovation Forum

ToR WHO WG on Vx Core protocol

ToR WHO WG on Vx R&D

ToR WHO WG on Animal models

ToR WHO WG on Assays

15 Jan 2021
Knowledge gaps & research priorities

06 Dec 2021
Further Vx research to achieve the control of the pandemic everywhere

29 Nov 2021
Assays and animal models

24 Jan X reactivity with other CoVs

27 Jan X reactivity between nCoV and SARS

30 Jan Vx Prioritization for CI trials

Progress summary: Animal models
20 Mar 2020 (27Feb-15 Mar 2020)
04 Apr 2020 (15-26 Mar 2020)
04 Jun 2020 (26 Mar-01Jun 2020)

Progress summary: Assays
05 May 2020 (18 Mar-01Apr 2020)

25 Oct 2021
Emerging evidence on additional doses & their safety

13 Aug 2021
Can booster doses contribute to control this pandemic: what research is needed?

How can reliance help in case of public health emergency?

Facilitate authorization or emergency use authorization

based on WHO PQ EUL or stringent regulatory authorities approvals

Encourage use of reliance and work-sharing

(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.)

Avoid retesting through **reliance** on the batch release testing from releasing NRAs/NCLs

Emergency regulatory authorizations issued by >150 LMI countries/territories

World Health Organization

update: as of 18 May 2022

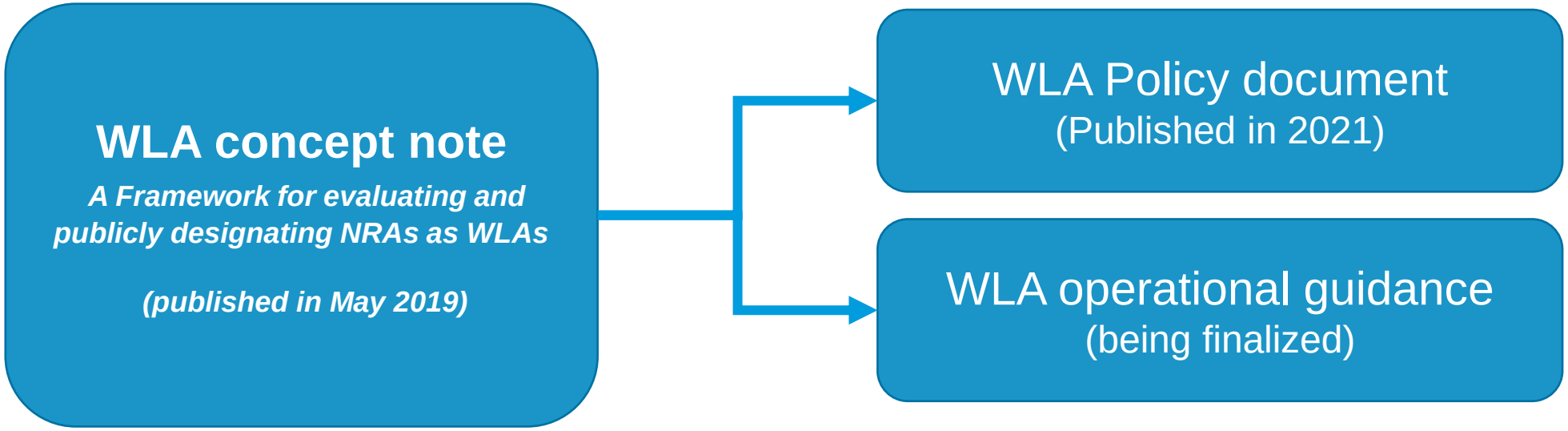
mRNA	Viral vector				Inactivated				Recombinant adjuvanted

Pfizer COMIRNATY	**Moderna** SPIKEVAX	**AZ** VAXZEVRIA	**SII** COVISHIELD	**Janssen** Covid-19 Vx	**CanSino** Convidecia	**Sinopharm** BIBP Covid-19 Vx	**Sinovac** CoronaVac	**Bharat** Covaxin	**Novavax** Nuvaxovid	**SII** Covovax
314 regulatory clearance **in 162** country/territory	**506** regulatory clearance **in 78** country/territory	**1'364** regulatory clearance **in 142** country/territory	**147** regulatory clearance **in 114** country/territory	**807** regulatory clearance **in 115** country/territory	**1** regulatory clearance **in 1** country/territory	**81** regulatory clearance **in 80** country/territory	**91** regulatory clearance **in 61** country/territory	X On suspension 02 Apr 2022	**34** regulatory clearance **in 34** country/territory	**1** regulatory clearance **in 1** country/territory
Shared EUL reports with **60 NRAs**	Shared EUL reports with **51 NRAs**	Shared EUL reports with **81 NRAs**	Shared EUL reports with **58 NRAs**	Shared EUL reports with **67 NRAs**	EUL granted 18 May 2022	Shared EUL reports with **60 NRAs**	Shared EUL reports with **47 NRAs**	Shared EUL reports with **17 NRAs**	Shared EUL reports with **20 NRAs**	Shared EUL reports with **9 NRAs**
4 DS sites 12 DP sites	2 DS sites 3 DP sites	8 DS sites 12 DP sites	2 DS sites 2 DP sites	3 DS sites 7 DP sites	1 DS sites 1 DP sites	1 DS site 1 DP site	1 DS site 1 DP site	1 DS site 1 DP site	2 DS sites 1 DP site	2 DS sites 2 DP sites
Ref NRA: • EMA • US FDA	Ref NRA: • EMA • US FDA • MFDS	Ref NRA: • EMA • MFDS • MHLW • TGA • DS: COFEPRIS • DP: ANMAT	Ref NRA: • DCGI	Ref NRA: • EMA • US FDA	Ref NRA: • NMPA	Ref NRA: • NMPA	Ref NRA: • NMPA	Ref NRA: • DCGI	Ref NRA: • EMA	Ref NRA: • DCGI

DS: Drug substance / DP: Drug product

Operationalizing WHO Listed Authorities (WLAs)

The WLA Framework



The WLA framework is envisaged to be operational in 2022

Definition of WLA: Adopted by the ECSPP in October 2020, TRS 1033

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 established benchmarking and performance evaluation process

Benefits of WHO-Listed Authority (WLA) framework

Enable efficient use of regulatory resources

by providing a robust framework to promote **trust, confidence** and **reliance**

Encourage continuous improvement of regulatory systems and

regulatory convergence

Help procurement decisions

on medical products by UN and other agencies, as well as countries (especially LMICs)

Contributes to WHO PQ programme

by expanding the pool of trusted regulatory authorities

Fosters health equity

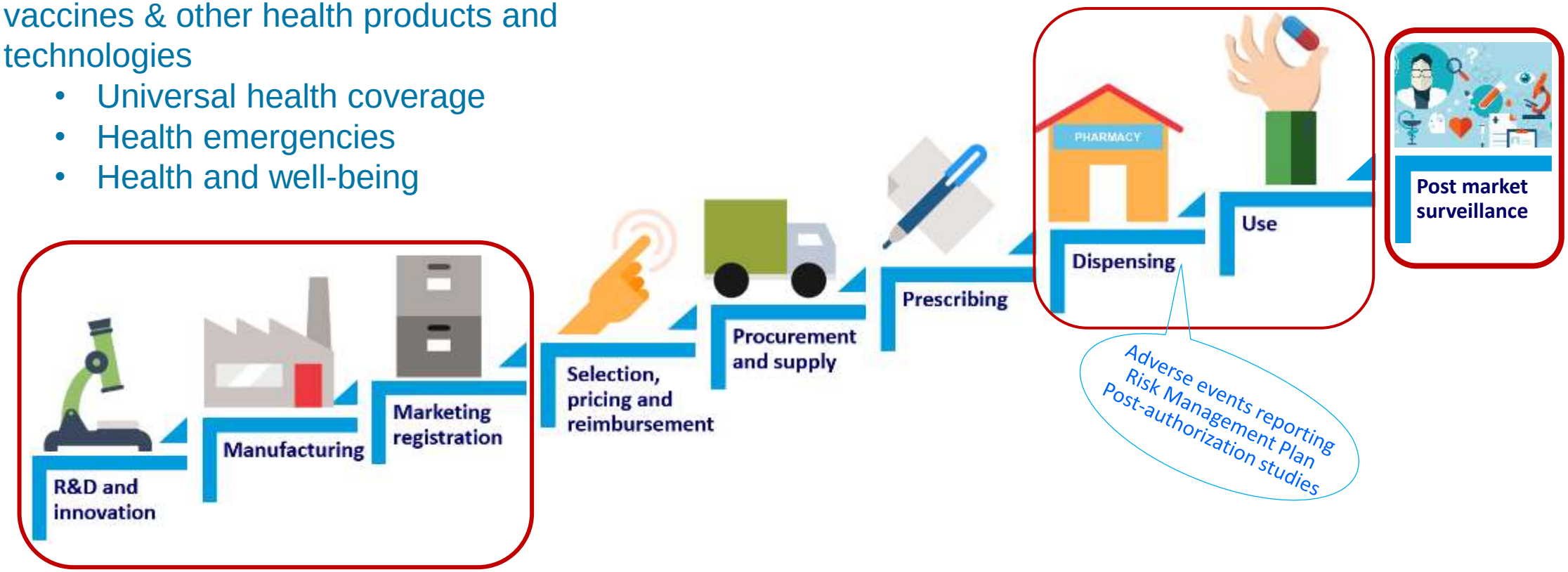
by enabling an environment for innovation and local production, and accelerating access to medical products

“End-to-end” health products’ management: shared responsibilities

Legislation, regulation, governance, monitoring

Access to quality-assured medicines, vaccines & other health products and technologies

- Universal health coverage
- Health emergencies
- Health and well-being

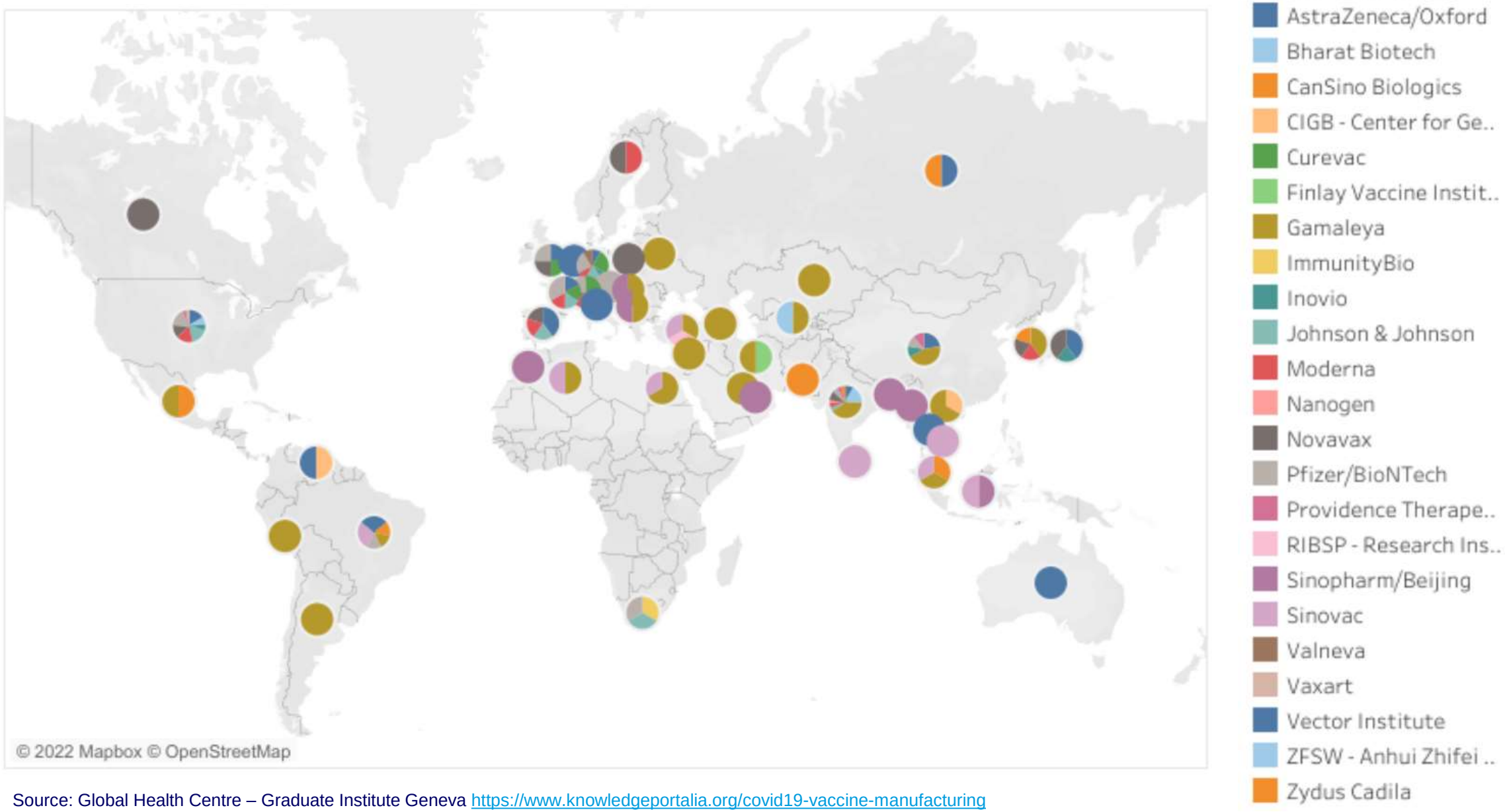


Joint reviews & assessments of clinical trials

Long term Good Regulatory Practice

Regulatory Reliance, Collaboration and Harmonization

Locations of Covid-19 Vaccine Manufacturers



Source: Global Health Centre – Graduate Institute Geneva https://www.knowledgeportalia.org/covid19-vaccine-manufacturing

Local Production and Assistance

WHO VACCINE MANUFACTURING WORKSHOP for SOUTHEAST ASIAN and WESTERN PACIFIC REGIONS

ONGOING PQ/EUL-RELATED SPECIALIZED TECHNICAL ASSISTANCE

MEMBER STATE SUPPORT IN STRENGTHENING LOCAL PRODUCTION

DZA, EUC, EGY, ETH, GHA, KAZ, NGA, SEN, SRB, etc.

IMPLEMENTATION OF WORLD LOCAL PRODUCTION FORUM RECOMMENDATIONS

Access to quality medicines and other health products requires **an integrated approach** with all stakeholders

World Health Organization

WORKING TOGETHER

Rogério Gaspar ¦ Director, Department of Regulation and Prequalification (RPQ)