RPQ Vision: essential role in ensuring Universal Health for All

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

Joint UNICEF-UNFPA-WHO meeting with manufactures and suppliers

08 March 2022

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

Access to Medicines and Health Products (MHP)

ADG - Mariângela Simão

World Health Organization

Health Products Policy and Standard (HPS)
Clive Ondari

Regulation and Prequalification (RPQ)
Rogério Gaspar

Prequalification (PQT)
Deus Mubangizi

- Office of the Unit Head
- Inspection Services — **Joey Gouws**
- IVD Assessment — **Irena Prat**
- Medicines Assessment — **Matthias Stahl**
- Vaccines & Immunization Devices Assessment — **Carmen Rodriguez**
- Vector Control Products Assessment — **Marion Law**
- Medical Devices — **TBD**

Regulation and Safety (REG)
Hiiti Sillo

- Office of the Unit Head
- Regulatory Systems Strengthening — **Alireza Khadem Broojerdi* & ****
- Regulatory Convergence and Networks — **Samvel Azatyan**
- Facilitated Product Introduction — **Samvel Azatyan*&****
- Laboratory Network and Services — **Gaby Vercauteren**
- Pharmacovigilance — **Shanthi Pal**
- Incidents and SF Medical Products — **Rutendo Kuwana**

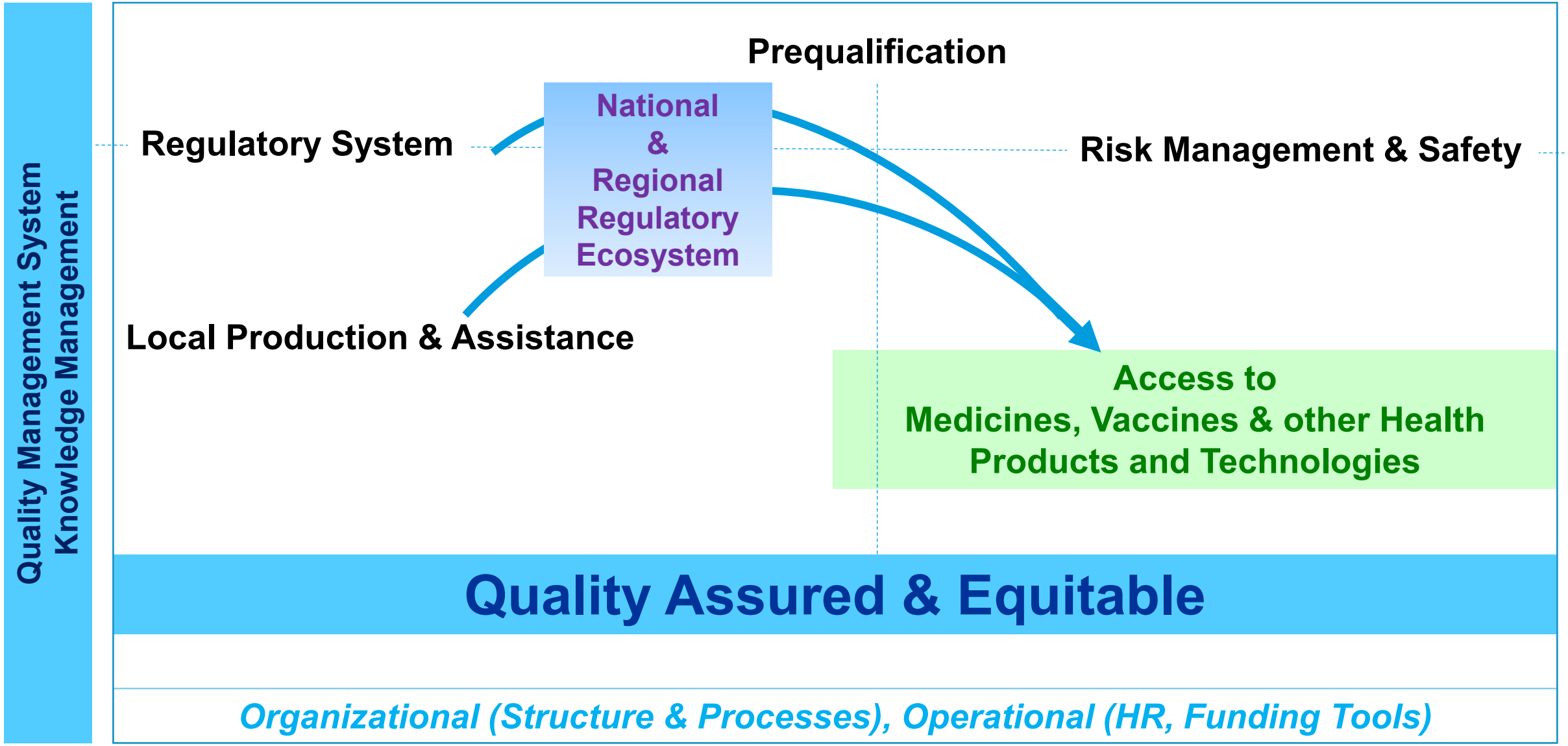
Local Prod. & Assist. (LPA)
Jicui Dong

Office of the Director

- 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/

RPQ Quality Management System (QMS)

Moving towards a single RPQ-wide QMS in compliance with *ISO9001:2015 standards*

from teams with differently structured operational QMS to a single harmonized QMS

2nd half 2021	✓	Developed Quality Policy and Quality Manual with quality objectives based on GPW13 and RPQ Strategic plan 2019-2023
1st half 2022	❑	Developing overarching general and administrative SOPs
1st half 2022	❑	Determining cross-cutting and team-specific SOPs • Cross-cutting SOPs to be 'owned' by relevant teams with associated KPIs
2nd half 2022 to 1st half 2023	❑	Developing cross-cutting and team-specific SOPs
As SOPs are introduced	❑	Implementation through generic training, on-the-job coaching and continuous improvement mechanisms, particularly: • change management • quality management review • internal audit

A reminder: WHO Regulatory Activities

Ensuring normative and technical excellence drives impact at country level

World Health Organization

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

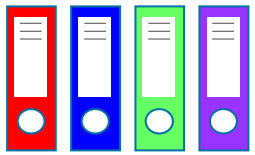
- Assure safety, quality efficacy & appropriateness of medical products used in LMICs, including medicines, vaccines, medical devices, cold chain equipment, vector control products & in vitro diagnostics
- Increase competition to shape the market

Regulation & Safety

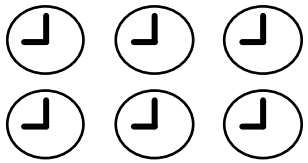
- Strengthen regulatory systems in countries and regions
- Increase knowledge of real-life adverse events and coordinate actions taken against adverse events
- Mitigate risks and protect against substandard / falsified products

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



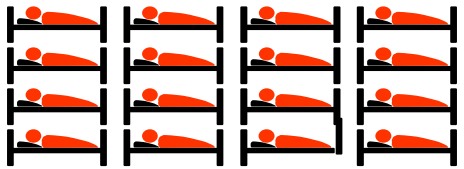
Decreased regulatory burden



Reduced time for regulation

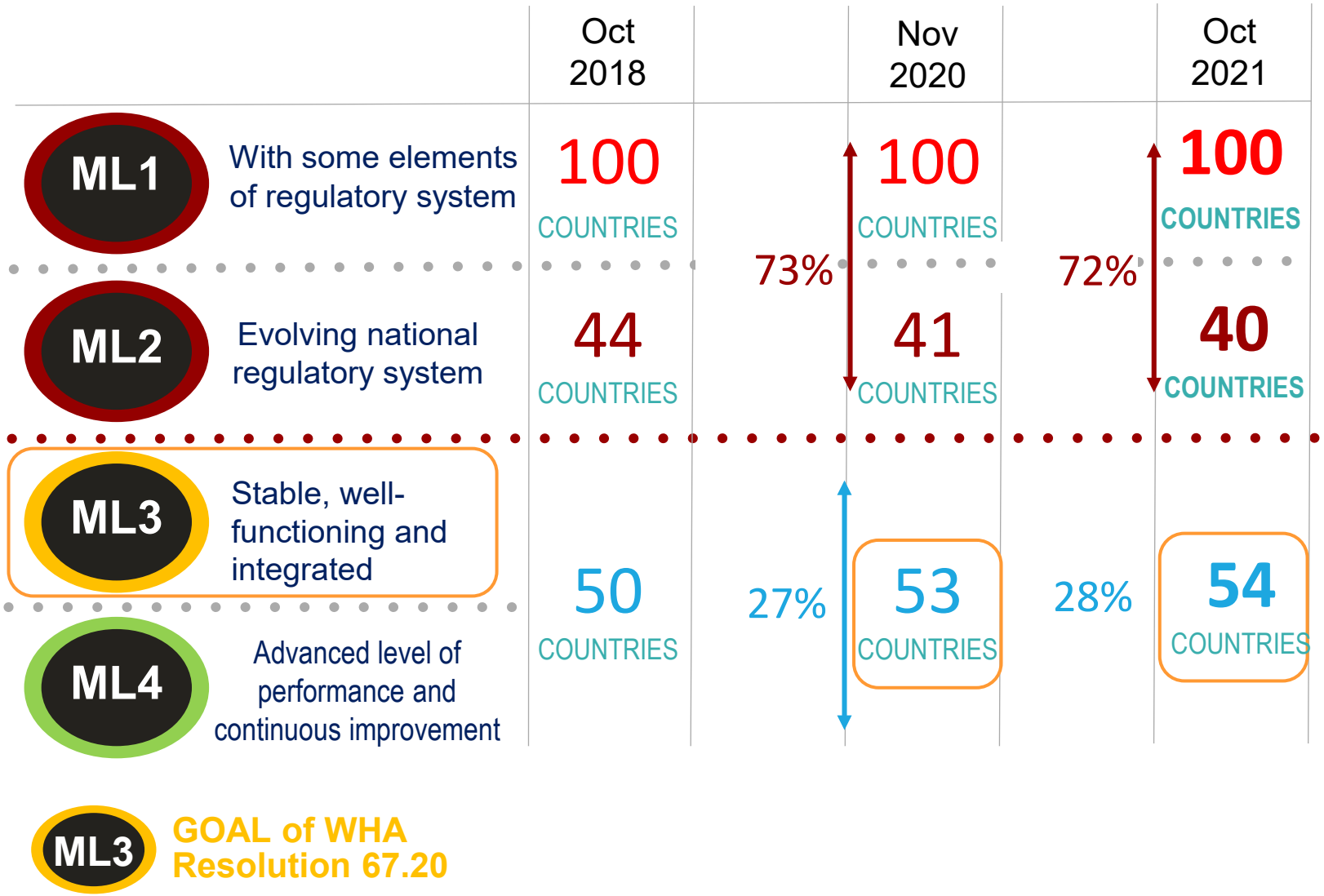
Increased regulatory capacity in LMIC

Decreased cost of regulation



Reduced mortality and morbidity

>70% of countries have weak national regulatory systems



ML3 **GOAL of WHA Resolution 67.20**

ML: (regulatory system) maturity level

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 highest maturity level in WHO classification (28 Feb 2022)

Background to WHO-Listed Authority (WLA)

01 To provide a transparent and evidence-based pathway for Regulatory authorities to be globally recognized

02 To promote access and the supply of safe, effective and quality medical products

03 To optimize use of limited resources by facilitating reliance

Policy document:

The Policy describes the purpose, definitions and high-level operating principles related to the evaluation and public listing of authorities

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

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

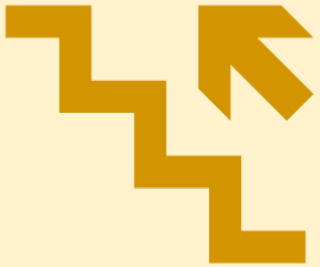
by expanding the pool of trusted regulatory authorities

Fosters health equity

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

Transitional Arrangements: *OBJECTIVES*

World Health Organization



Recognize the achievements and work of all RAs on the Interim lists

Protect the global supply of prequalified products

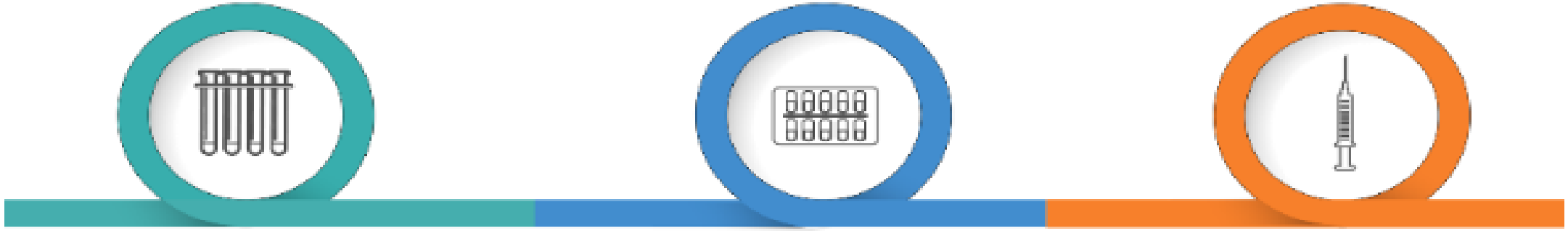
Provide a clear and transparent path forward for RAs on the Interim list that wish to become WLAs

Ensure processes are feasible and efficient with respect to WHO and RAs capacity

PRINCIPLES AND KEY STEPS OUTLINED IN THE DRAFT DOCUMENT
A 5 YEAR PERIOD

Increase regulatory convergence and harmonization

- WHO guidance on Good regulatory and reliance practices
- Implementation guidance on quality management systems for NRAs
- Sharing information / expertise: (assessment, inspection and testing results or expertise) that serve as basis for national decisions – avoiding duplication
- Voluntary participation – reference authorities, participating authorities and manufacturers/sponsors



WHO Collaborative Registration Procedure (CRP)

- Vaccines: 2004
- Medicines: 2012
- HIV medicines Pilot: Nov 2018 as CRP-Lite with FDA
- Diagnostics: Pilot 2019
- Vector control: Pilot 2020

Facilitated Registration "SRA" CRP

- Initiated in 2015 EMA and MHRA with 20 African NRAs

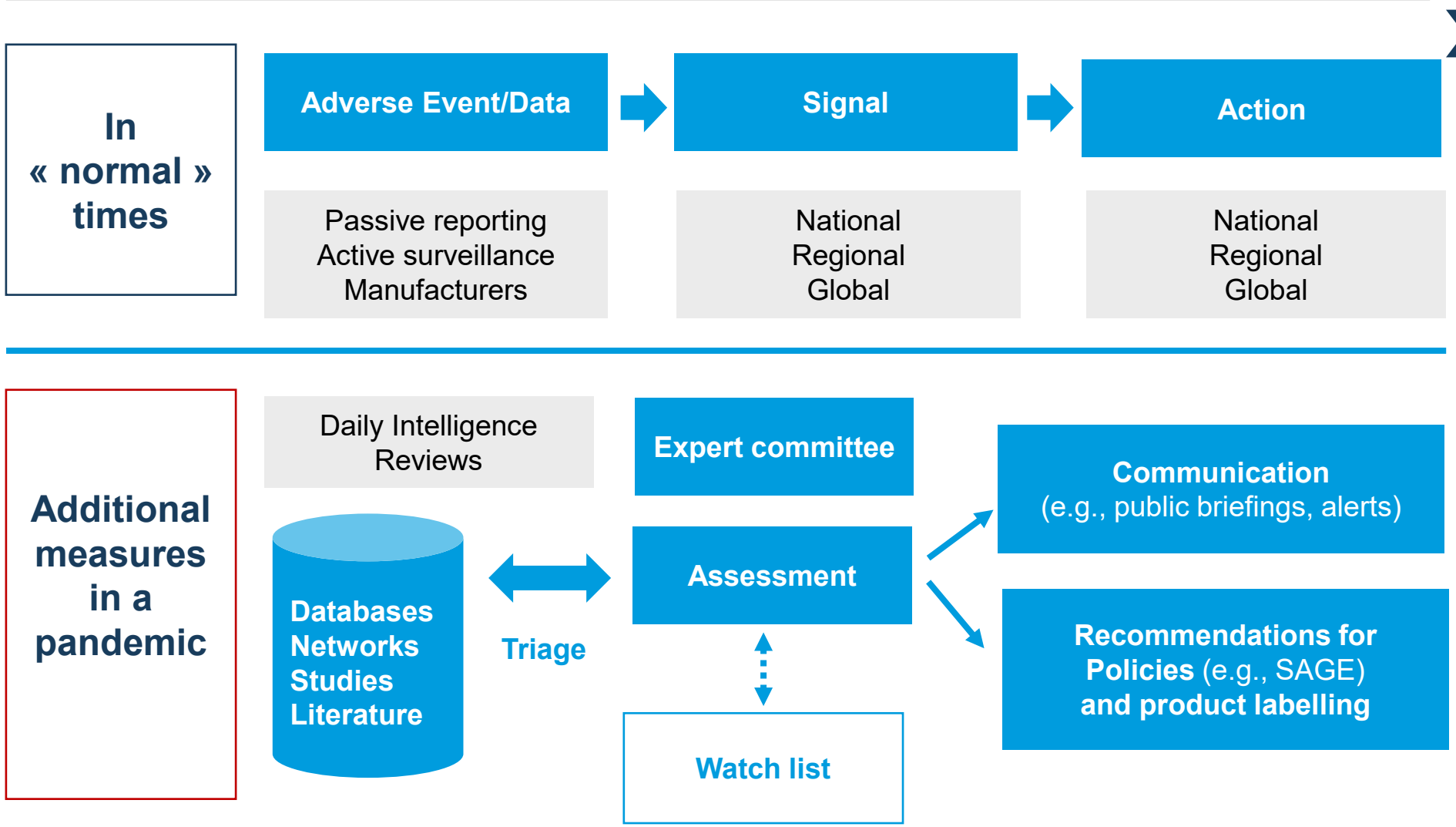
Regional networks

- AVAREF
- AUDA-NEPAD
- ASEAN SIAHR project
- CARPHA
- ZAZIBONA

Pharmacovigilance System at work

World Health Organization

Safety surveillance of vaccines



Key take-aways

- **More pro-active**
- **Enabling real-time data collection and assessment**
- **Leveraging more data sources** (incl. informal sources such as social networks)
- **Greater coordination and joint action** (e.g., through regulatory networks)
- **Ongoing evaluation and adjustment** to meet evolving needs

RPQ Strategic priorities:

1

SP 1:

Strengthen country and regional regulatory systems

2

SP 2:

Improve regulatory preparedness for public health emergencies

3

SP 3:

Reinforce and expand WHO prequalification and product risk assessment

4

SP 4:

Increase the impact of WHO regulatory support activities

Overview of SARS-CoV-2 IVDs: WHO EUL status as of 21 Feb 2022

IVD products	Total #	Nucleic acid	Antigens	Antibodies
EOIs	172	69	62	41
Active Applications	51	18	33	On hold
Awaiting dossier	6	2	4	
Dossier received	45	16	29	
• Pre-screening		2	1	
• Screening		5	12	
• Under assessment		9	16	
In renewal process		19	3	1
Not Renewed		2*	0	0
EUL listed	**30 (-2)**	**24 (-2)**	**5**	**1**
EUL not accepted	**61**	**27**	**24**	**10**

Activity 01 – 21 Feb 2022	
Dossier screening Round 1 completed	11
Dossier screening Round 2 completed	3
Dossiers for review by assessors	4 ★
Applications closed at screening	5
EUL listed	1

★ 4 dossiers under review by assessors at HSA Singapore & PEI Europe

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

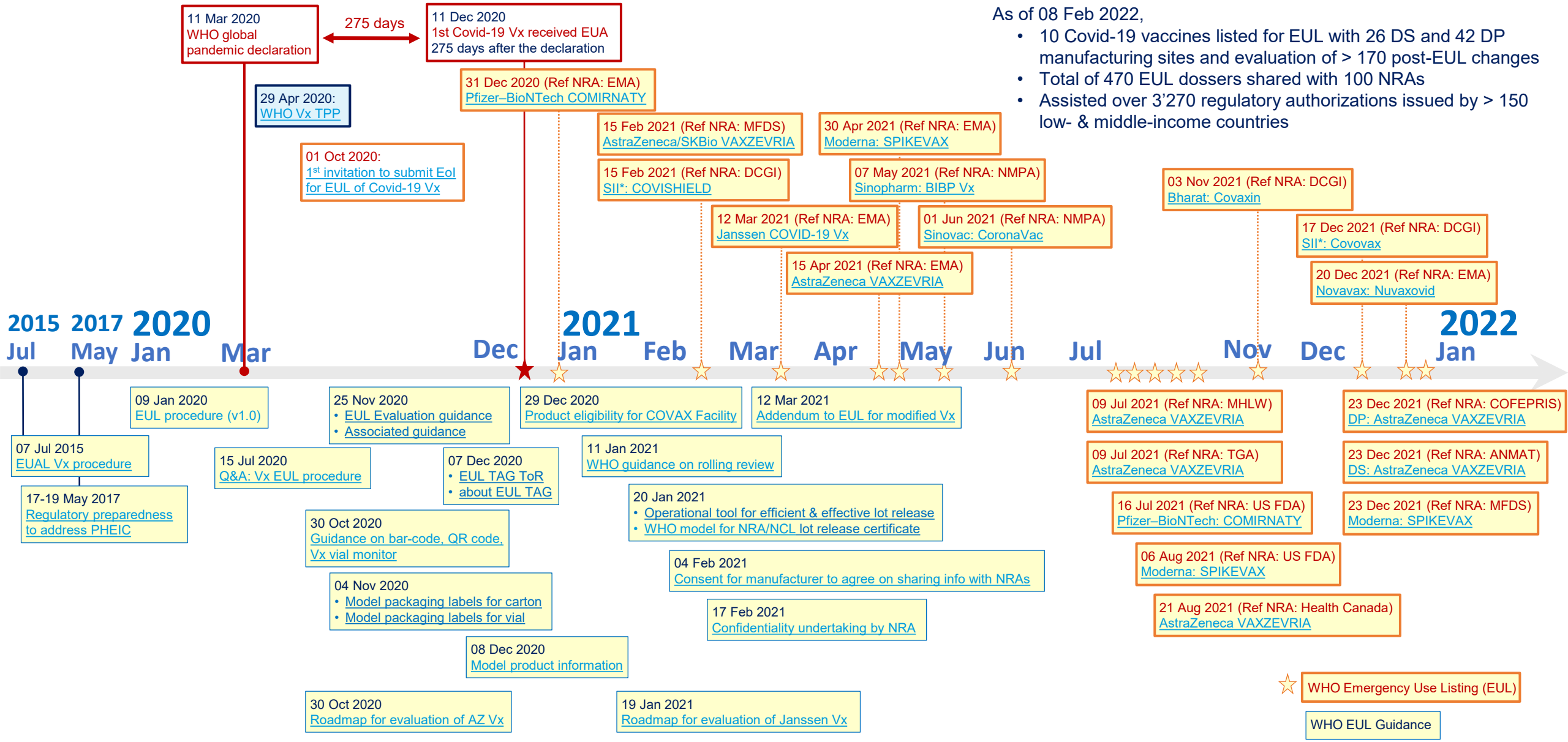
Progress summary: Animal models
20 Mar 2020 (27Feb-15 Mar 2020)
04 Apr 2020 (15-26 Mar 2020)
04 Jun 2020 (26 Mar-01Jun 2020)

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?

Timeline of events: WHO Emergency Use Listing (EUL) of Covid-19 vaccines



As of 08 Feb 2022,

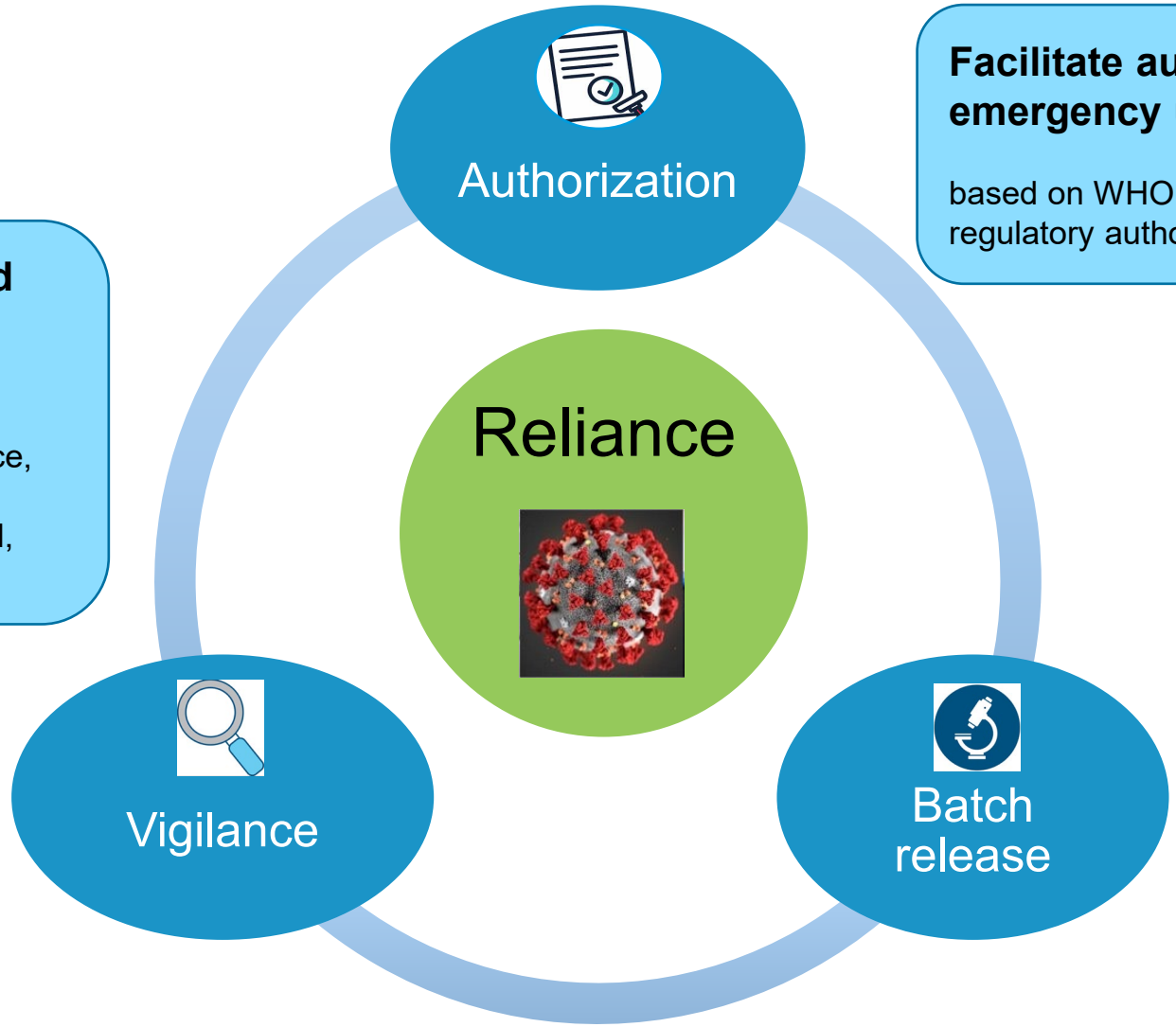
- 10 Covid-19 vaccines listed for EUL with 26 DS and 42 DP manufacturing sites and evaluation of > 170 post-EUL changes
- Total of 470 EUL dossers shared with 100 NRAs
- Assisted over 3'270 regulatory authorizations issued by > 150 low- & middle-income countries

*SII: Serum Institute of India

How can reliance help in case of public health emergency?

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.)



Facilitate authorization or emergency use authorization

based on WHO PQ EUL or stringent regulatory authorities approvals

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

Emergency regulatory authorizations issued by >150 LMI countries/territories

update: as of 25 February 2022

mRNA	Viral vector	Inactivated	Recombinant adjuvanted

Pfizer COMIRNATY	**Moderna** SPIKEVAX	**AZ** VAXZEVRIA	**SII** COVISHIELD	**Janssen** Covid-19 Vx	**Sinopharm** BIBP Covid-19 Vx	**Sinovac** CoronaVac	**Bharat** Covaxin	**Novavax** Nuvaxovid	**SII** Covovax
299 regulatory clearance	**502** regulatory clearance	**1'331** regulatory clearance	**140** regulatory clearance	**795** regulatory clearance	**80** regulatory clearance	**90** regulatory clearance	**1** regulatory clearance	**34** regulatory clearance	**1** regulatory clearance
in 156 countries/territories	**in 78** countries/territories	**in 142** countries/territories	**in 114** countries/territories	**in 115** countries/territories	**in 80** countries/territories	**in 61** countries/territories	**in 1** country/territory	**in 34** countries/territories	**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**	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 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: • DCGI	Ref NRA: • EMA	Ref NRA: • DCGI

DS: Drug substance / DP: Drug product

Assessment, monitoring, and adjustments to variants is critical

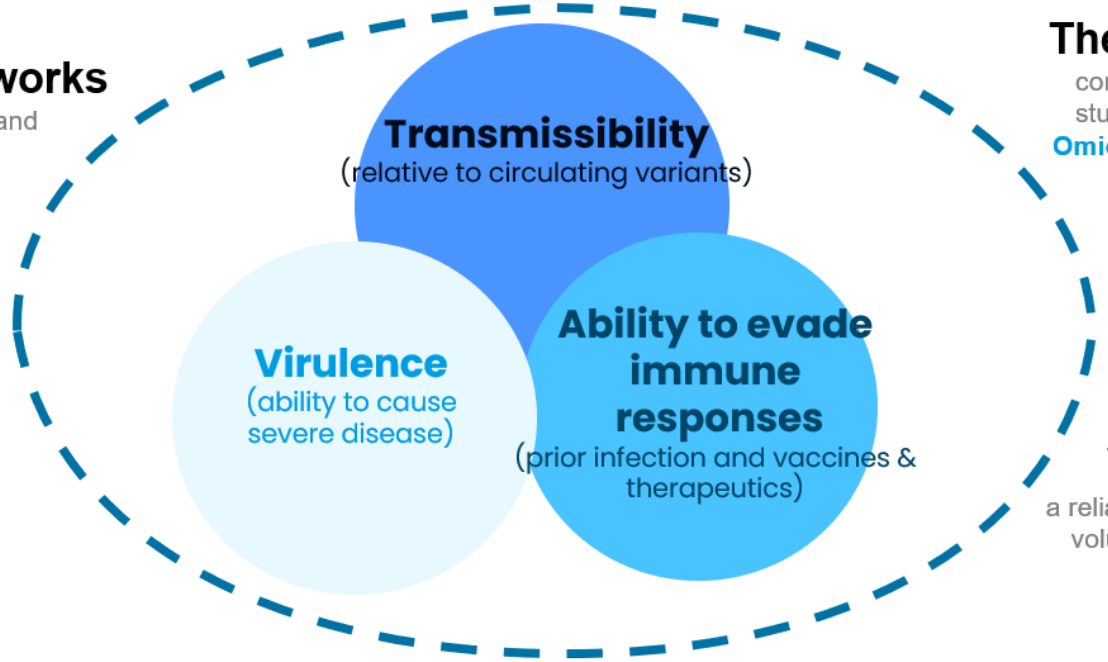
World Health Organization

TAG for SARS-CoV-2 Virus Evolution
is assessing its effect on transmission, disease severity, vaccines, therapeutics and diagnostics, and the effectiveness of PHSMs

WG for Clinical Management Networks
is assessing impacts of VOCs on current vaccines and
WHO Global Clinical Platform for COVID

The Joint Advisory Group on Therapeutics Prioritization
is analyzing the possible effects on treatment of hospitalized patients.

WG on outpatient platform trials
is reviewing trial designs and challenges



The R&D Blueprint for Epidemics is
convening researchers to identify knowledge gaps, and studies needed to answer the most pressing questions.
Omicron variant assays & animal models study tracker

The WG on vaccines TPPs
is reviewing current desirable and minimum criteria for vaccines.

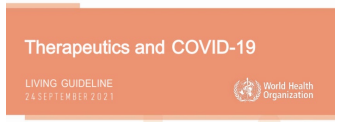
WHO BioHub system
a reliable, safe, and transparent mechanism to voluntarily share novel biological materials

TAG for COVID-19 Vaccine Composition*
Is assessing impacts of VOCs on current vaccines and determining whether changes to the composition of vaccines are needed.

SAGE on Vaccines & Immunization
is reviewing data to develop evidence based recommendations on the vaccination policies and target populations.

Thousands of researchers around the world are contributing data and expertise to the deliberations

*Interim Statement on COVID-19 vaccines in the context of the circulation of the Omicron SARS-CoV-2 Variant from the WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) https://www.who.int/news/item/11-01-2022-interim-statement-on-covid-19-vaccines-in-the-context-of-the-circulation-of-the-omicron-sars-cov-2-variant-from-the-who-technical-advisory-group-on-covid-19-vaccine-composition



WHO Therapeutics and COVID-19: Living Guideline*

Latest update issued on 03 March 2022

*WHO Therapeutics and COVID-19: Living Guideline

World Health Organization

2022 03 03	conditional recommendation for use of Molnupiravir **	for patients with non-severe COVID-19, conditional for those at highest risk of hospitalization
	conditional recommendation to use a combination of neutralizing monoclonal antibodies (casirivimab and imdevimab) **	on-severe COVID-19 patients at the highest risk of severe disease
2022 01 14	strong recommendation for the use of baricitinib** as an alternative to interleukin-6 (IL-6) receptor blockers	patients with severe or critical COVID-19
	conditional recommendation against the use of ruxolitinib and tofacitinib	patients with severe or critical COVID-19
	conditional recommendation for the use of sotrovimab	patients with non-severe COVID-19, conditional for those at highest risk of hospitalization
2021 12 07	Strong recommendation against convalescent plasma	patients with non-severe COVID-19
	Recommendation not to use convalescent plasma	patients with severe or critical COVID-19 except in the context of a clinical trial
2021 09 24	conditional recommendation to use a combination of neutralizing monoclonal antibodies (casirivimab & imdevimab)**	severe and critically ill COVID-19 patients with seronegative status
2021 07 06	strong recommendation to use IL-6 receptor blockers (tocilizumab or sarilumab)**	patients with severe or critical COVID-19
2021 03 31	recommendation not to use ivermectin	patients with COVID-19 except in the context of a clinical trial
2020 12 17	strong recommendation against hydroxychloroquine	patients with COVID-19 of any severity
	strong recommendation against lopinavir/ritonavir	patients with COVID-19 of any severity
2020 11 20	conditional recommendation against remdesivir	hospitalized patients with COVID-19
2020 09 02	strong recommendation for systemic corticosteroids**	patients with severe and critical COVID-19
	conditional recommendation against systemic corticosteroids	patients with non-severe COVID-19

**Expression of interest for Prequalification

Therapeutics: EOI for PQ / ERP

(as of 11 Feb 2022)

World Health Organization

Original products approved by SRA and generic/biosimilar are invited		EoI issued	PQ status
Direct-acting antivirals	Nirmatrelvir 150 mg tablets plus ritonavir 100 mg tablet, co-packaged for oral administration	17 Dec 2021	Meeting with one manufacturer
	Molnupiravir* 200 mg capsules for oral administration	15 Nov 2021	4 applications for API under assessment
Neutralizing antibodies	Sotrovimab solution for infusion, 500 mg/8ml Baricitinib 2 mg tablets	25 Nov 2021	
Janus kinase inhibitors	Baricitinib 2 mg tablets	14 Jan 2022	
corticosteroid	Dexamethasone** • tablet, 1.5mg, 2mg, 6mg • oral solution, 2mg/5ml or 10mg/5ml, as the base orsodium phosphate • solution for injection, 3.3mg/ml or 6.6mg/ml, as thesodium phosphate	10 July 2020	PQed products: 4 FPPs 2 APIs 2 for injection (Sep & Dec 2021)
IL-6 inhibitors	Tocilizumab IV 20mg/ml for further dilution	19 May 2021	11 Feb 2022: 3x 20mg/ml prequalified
	Sarilumab 200mg/ml 1.14 ml for further dilution prior to IV Sarilumab 150mg/ml 1.14 ml for further dilution prior to IV	19 May 2021	

Abridged assessment will be used for products approved by SRA

* for generic products, Global Fund issued a call for Expert Review Panel (ERP) on 09 Dec 2021

Where do we go from here?

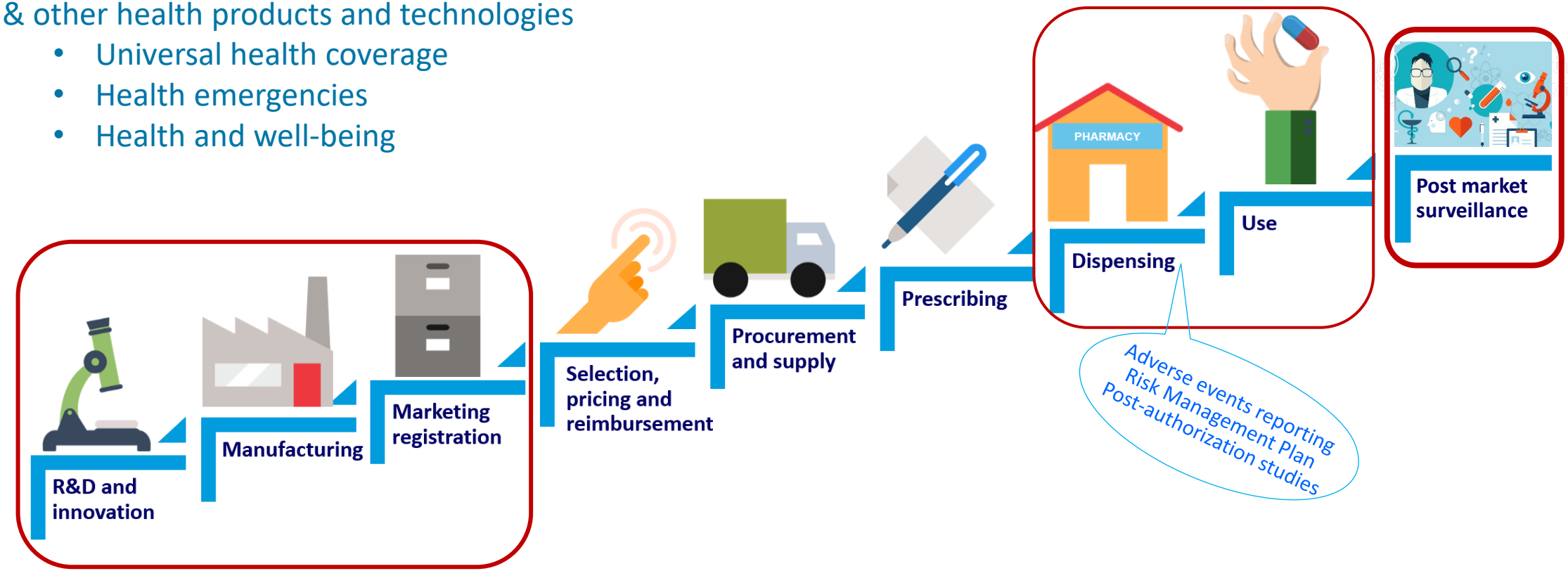
“End-to-end” health products’ management: shared responsibilities

World Health Organization

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

Local Production and Assistance

WHO VACCINE MANUFACTURING WORKSHOP for SOUTHEAST ASIAN and WESTERN PACIFIC REGIONS

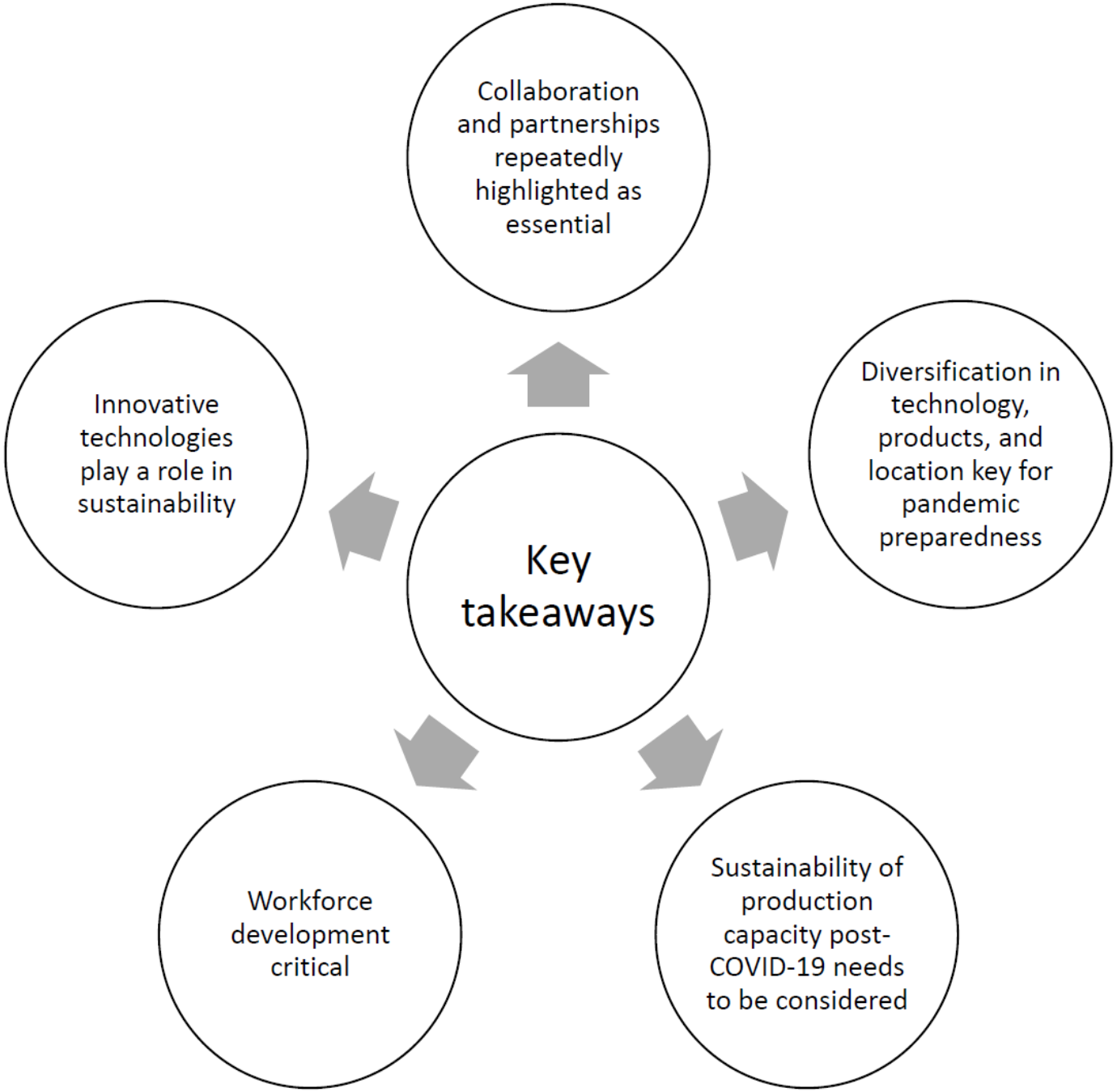
ONGOING PQ/EUL-RELATED SPECIALIZED TECHNICAL ASSISTANCE

MEMBER STATE SUPPORT IN STRENGTHENING LOCAL PRODUCTION

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

IMPLEMENTATION OF WORLD LOCAL PRODUCTION FORUM RECOMMENDATIONS

World Local Production Forum (WLPF)



Covid has provided important lessons

- Since early 1960s, national regulations have been built as stand-alone systems, but
- Covid-19 pandemic has brought many stakeholders to work together, enabling **cooperation**, allowing for increased standards **convergence** and promoting **reliance** concepts in regulatory as well as public health thinking

Taking this opportunity and lessons learned so far to:

- further elaborate **cooperative and flexible** approaches
- respect **international standards and best practices**, and
- adopt an approach that focuses on what cannot be done by others while leveraging the work of other trusted regulators and institutions for the rest

Where do we go from here?

WHO Mission:

- **Promote Health**
- **Keep the World Safe**
- **Serve the Vulnerable**

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

WORKING TOGETHER

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

backup

Regulatory convergence, harmonization, networking and reliance

- Technical assistance in establishment and operationalization of the African Medicines Agency (AMA) and continued support to AMRH Initiative
- Facilitation of production introduction in countries through CRP and in-country regulatory authorizations of COVID-19 vaccines & therapeutics
- Revision of the WHO Model Regulatory Framework for medical devices including *in vitro* diagnostics
- Support the implementation of GRP, GRelP, QMS guidelines by NRAs, including e-learning modules and reliance examples repository
- Global Competency Framework for Regulators

✓ continue support for online skills management system to facilitate ongoing pilot and updating draft competency framework for public consultation

Regulatory Systems Strengthening

Benchmarking of regulatory systems in priority countries

- ✓ Planned: Egypt, Republic of Korea, China, Kenya, Rwanda, Philippines, Turkey
- ✓ Follow up visits (towards ML 3): Nigeria, South Africa

Undertake capacity building and technical assistance in priority countries

- ✓ Includes Uganda, Sri Lanka, Senegal, Burkina Faso, Kazakhstan, others

WLA Framework - Operationalization

- ✓ Finalization of operational guidance, transitional arrangements of interim lists of NRAs

- Piloting the Research Ethics Committee tool & GBT+ medical devices & IVDs
- Strengthening regulatory capacity to respond to public health emergencies

CIP Network: operationalization and roll out to regions and countries

Challenges and lessons learned:

- Wide variety of platforms: 12 candidates under EUL assessment out of 144 candidates in clinical phase
- Managing an increasing number of post-EUL changes
  - Changes in stability data, formulation, storage condition, extension of shelf-life, etc. and corresponding changes in labeling and package insert
- Close intersectoral cooperation and collaboration at national, regional and international fora

- Building trust and confidence: key to implementation of reliance, effective and efficient authorization
- Frequent and open dialogues: assisting to achieve regulatory alignment and conversion
- Joint assessment / inspections: increasing efficiency

Vaccines currently under EUL assessment:

- CanSinoBio
- Clover
- Russian Direct Investment Fund
- WIBP Sinopharm
- Sanofi
- Zhifei Longcom
- Shifa Pharmed
- CureVac
- Vector state research centre of virology and biotechnology
- CIGB
- IMBCAMS,
- BioCubaFarma

https://extranet.who.int/pqweb/sites/default/files/documents/Status_COVID_VAX_18February2022.pdf