World Health Organization

Working together to build effective & efficient regulatory systems

Improving affordable & equitable access to quality-assured medical products

DCVMN-AGM2022

Session on Innovation in Regulatory & PQ

Rogério Gaspar ¦ Director, Department of 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

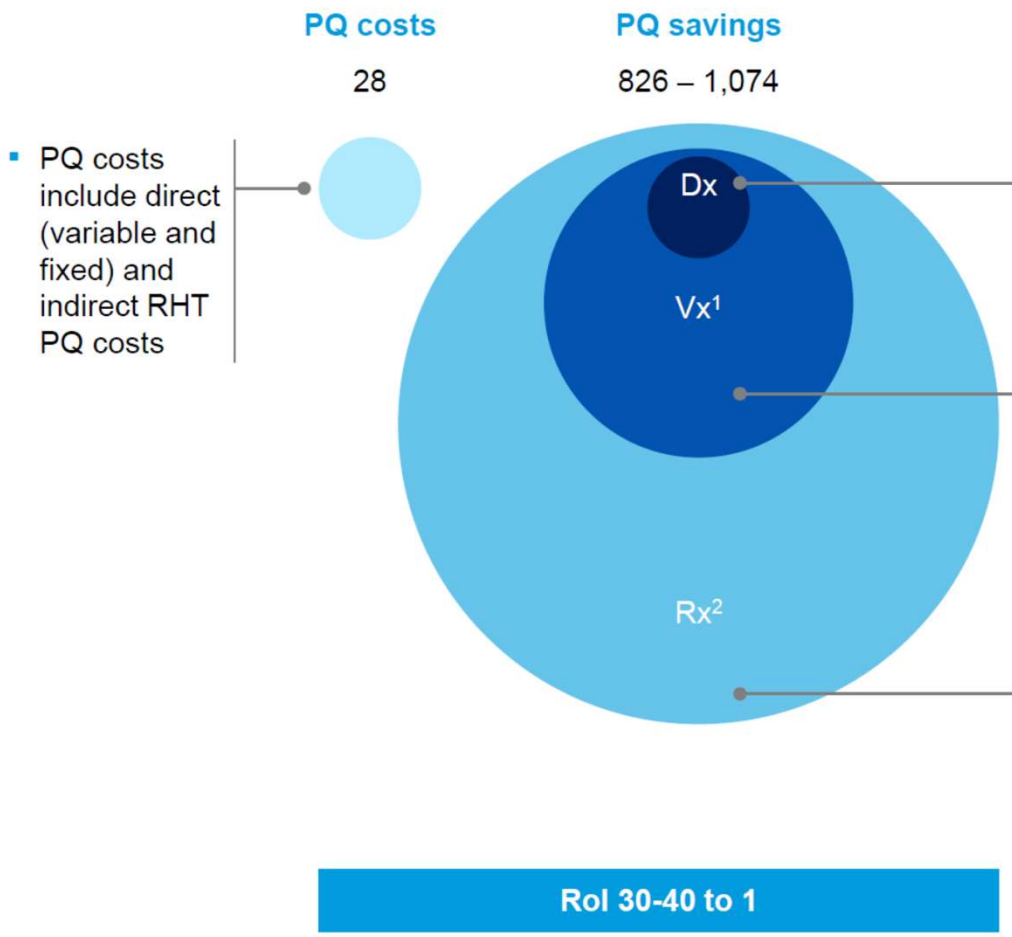
- ✓ Benchmarking and technical assistance to address regulatory gaps
- ✓ Promoting regulatory convergence, harmonization, work-sharing and reliance mechanisms
- ✓ Improving countries' ability to carry out risk-based post-marketing surveillance to securing supply chains against SF products
  - Includes 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/

4A WHO PQP has a Return on Investment of 30-40 to 1

USD Mn

VISUALIZATION NOT TO SCALE



- PQ costs include direct (variable and fixed) and indirect RHT PQ costs

- Limited unit price drop given each diagnostics method has 1 MNC with > 50% market share
- Conservative value as a limited time interval (2012-2014[2]) and only HIV diagnostics is considered

- Key driver is high volume
- DTP-HepB-Hib[3] accounts for majority of savings

- Rx-HIV and Rx-Malaria comprises > 80% of savings
  - Rx-HIV key driver is high volume
  - Rx-Malaria key driver is large unit price drop
- No savings Rx-RH considered despite injectables price drop, however these are mostly supplied by MNCs (90%+)

RoI 30-40 to 1

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Snapshot of donations/allocations (15 Aug 2022)

4926 regulatory approvals in 175 countries/territories

AstraZeneca (incl. SII)	Johnson & Johnson	Moderna	Pfizer	Sinopharm	Sinovac	Novavax
149 countries/territories	**131** countries/territories	**96** countries/territories	**175** countries/territories	**96** countries/territories	**77** countries/territories	**58** countries/territories
2061 regulatory clearance	**1057** regulatory clearance	**802** regulatory clearance	**723** regulatory clearance	**96** regulatory clearance	**129** regulatory clearance	**58** regulatory clearance
8 DS sites 12 DP sites	3 DS sites 7 DP sites	2 DS sites 3 DP sites	4 DS sites 10 DP sites	1 DS/DP site	1 DS/DP site	1 DS/DP site

Immunobridging

WHO EUL requirements updated March 2022

Revised guidance EUL document*

30 March 2022

- Posted on 30 March 2022, following discussions with regulators and with the WHO R&D Blueprint Team
- The revised document
  - Acknowledges applications for EUL based on *immunobridging*
  - Indicates that careful choice of comparators is important
  - Indicates that additional nonclinical and immunogenicity data may be required
  - Indicates that **demonstration of efficacy by in-deployment clinical trials** or of (more likely to happen in practice) **effectiveness by post-deployment observational studies** will also be needed as a post-listing commitment

Avoids being too prescriptive

Is aligned with the

- revised WHO Target Product Profiles (TPP) for COVID-19 vaccines
- draft R&D Blueprint Team "Framework" document

* **Considerations for evaluation of COVID-19 vaccines: Points to consider for manufacturers of COVID-19 vaccines. Revised version, 30 March 2022** (https://extranet.who.int/pqweb/sites/default/files/documents/Considerations_Assessment_Covid-19_Vaccines_v30March2022.pdf)

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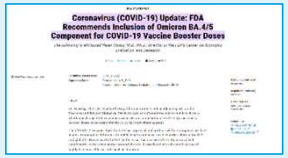
Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC)

The WHO TAG-CO-VAC continues to monitor and assess the **evidence on the genetic and antigenic characteristics of SARS-CoV-2 Variants of Concern (VOC)**, including descendent lineages of VOCs.

In their latest statement[1], TAG-CO-VAC advised that it may be prudent for manufacturers seeking to pursue an updated composition of current COVID-19 vaccines, to seek to **achieve broader immunity** against circulating and emerging variants, while **retaining protection against severe disease and death**

- **viruses or sequences closely related to Omicron BA.1** are some of the **most antigenically distant from the index virus**



The USA FDA issued a recommendation for COVID-19 vaccine composition to include Omicron BA.5 in an attempt to **increase and extend protection by better matching** the vaccine composition with circulating variants

- mRNA vaccines which include BA.5 **may be available in the USA by the Northern Hemisphere fall, pending regulatory approval.**

A statement from ICMRA[2] indicates that **adapted mRNA vaccines, which incorporate an Omicron variant,** can increase and extend protection, **when used as a booster dose,** but gives no indication as to which Omicron lineage should be included.

The MHRA has approved[3] the use of the Moderna bivalent vaccine product (index virus + Omicron BA.1) as a booster dose in the UK.

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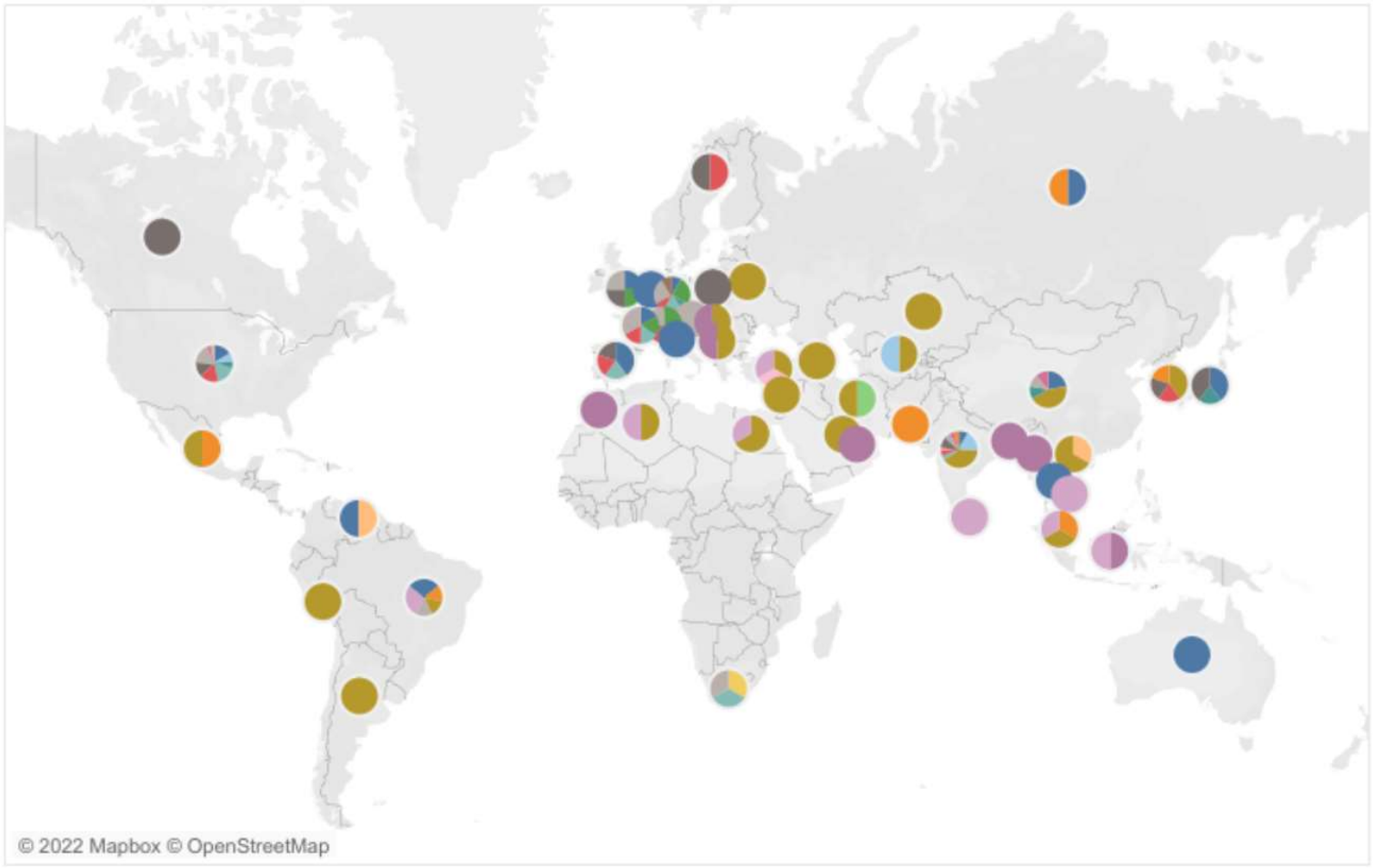
1. https://www.who.int/news/item/17-06-2022-interim-statement-on--the-composition-of-current-COVID-19-vaccines
2. International Coalition of Medicines Regulatory Authorities; https://icmra.info/drupal/en/covid-19/30june2022
3. https://www.gov.uk/government/news/first-bivalent-covid-19-booster-vaccine-approved-by-uk-medicines-regulator

Locations of Covid-19 Vaccine Manufacturers



Vaccine Developer1
- AstraZeneca/Oxford
- Bharat Biotech
- CanSino Biologics
- CIGB - Center for Ge..
- Curevac
- Finlay Vaccine Instit..
- Gamaleya
- ImmunityBio
- Inovio
- Johnson & Johnson
- Moderna
- Nanogen
- Novavax
- Pfizer/BioNTech
- Providence Therape..
- RIBSP - Research Ins..
- Sinopharm/Beijing
- Sinovac
- Valneva
- Vaxart
- Vector Institute
- ZFSW - Anhui Zhifei ..
- Zydus Cadila

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

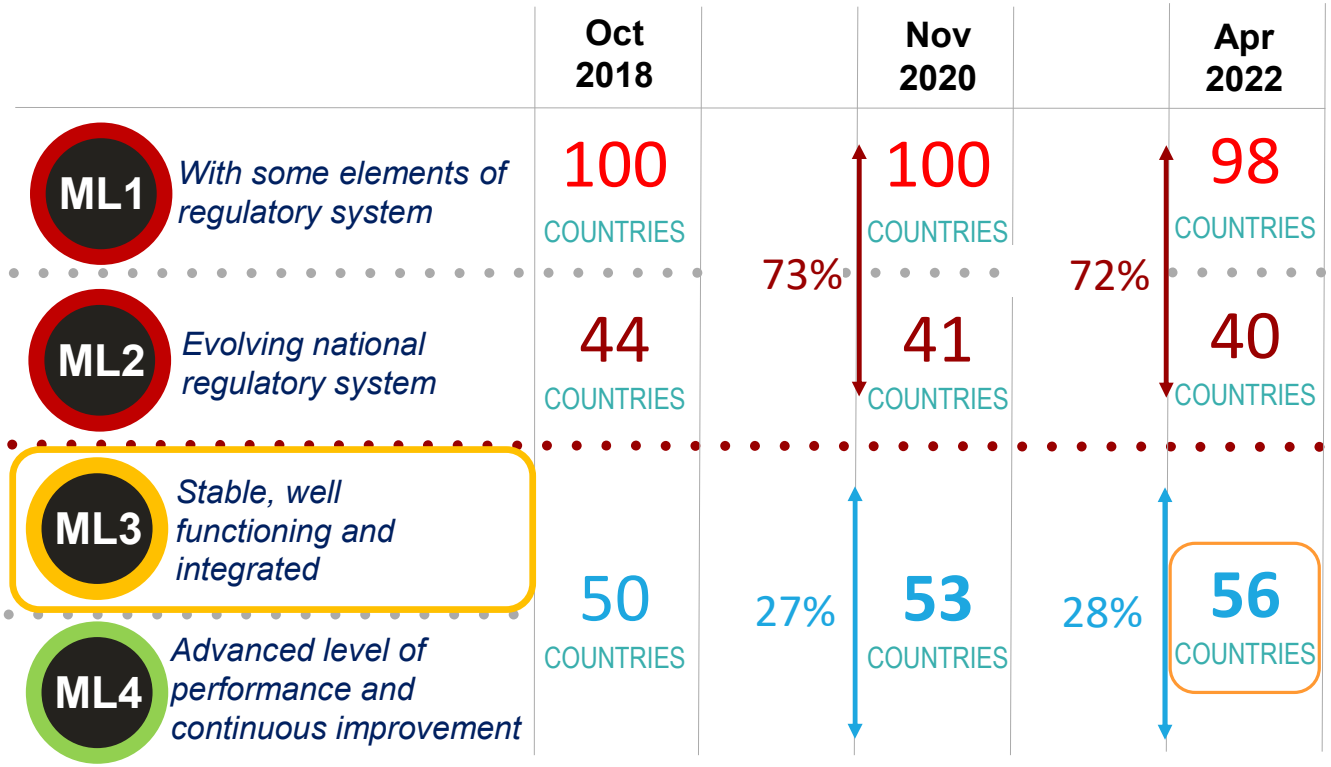
ONGOING PQ/EUL-RELATED SPECIALIZED TECHNICAL ASSISTANCE

MEMBER STATE SUPPORT IN STRENGTHENING LOCAL PRODUCTION

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

IMPLEMENTATION OF WORLD LOCAL PRODUCTION FORUM RECOMMENDATIONS

Global status of national regulatory systems, April 2022



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

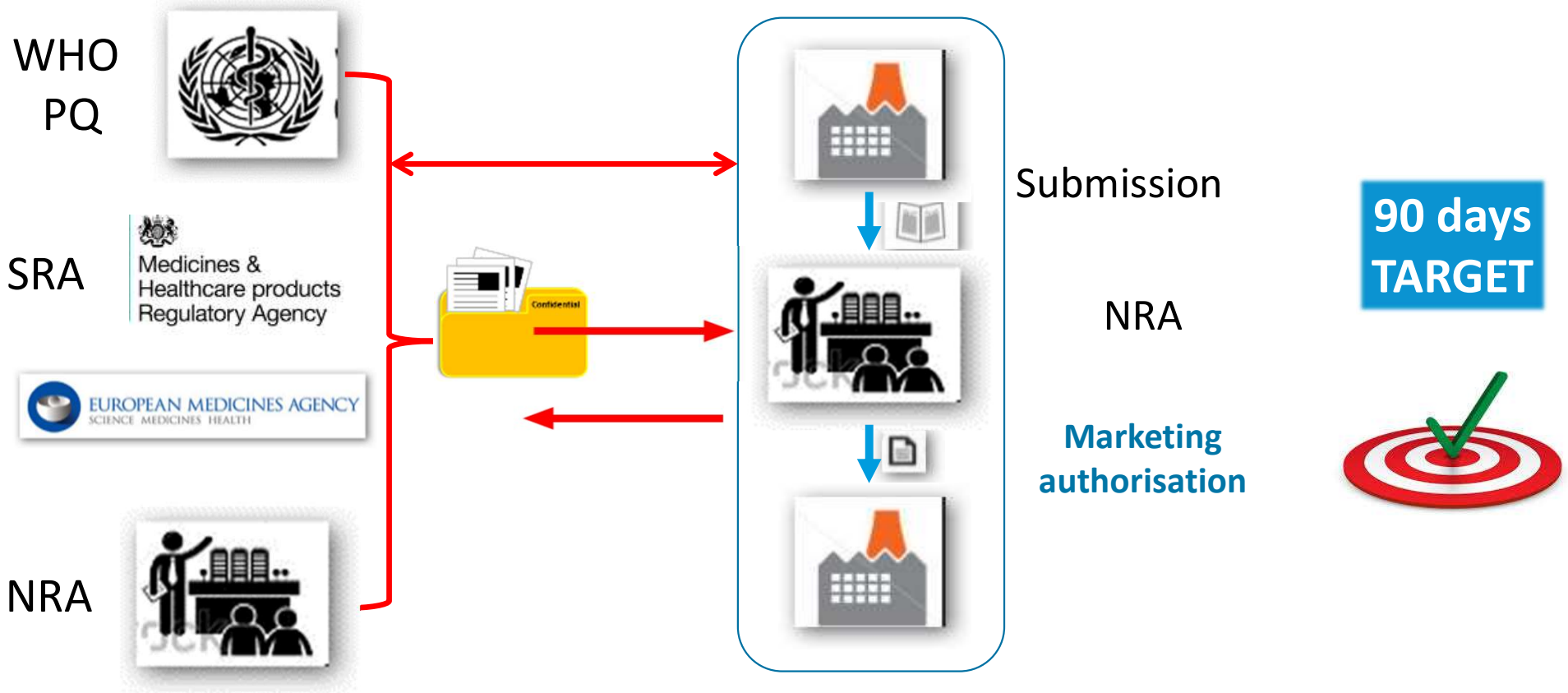
[Singapore medicines regulator world's first to achieve the highest maturity level (ML4) following assessment](#) (28 Feb 2022)

ML3 **GOAL of WHA Resolution 67.20**

Nigeria and Egypt announced as ML 3 in March 2022

ML: *(regulatory system) maturity level*

How does the collaborative procedures work?



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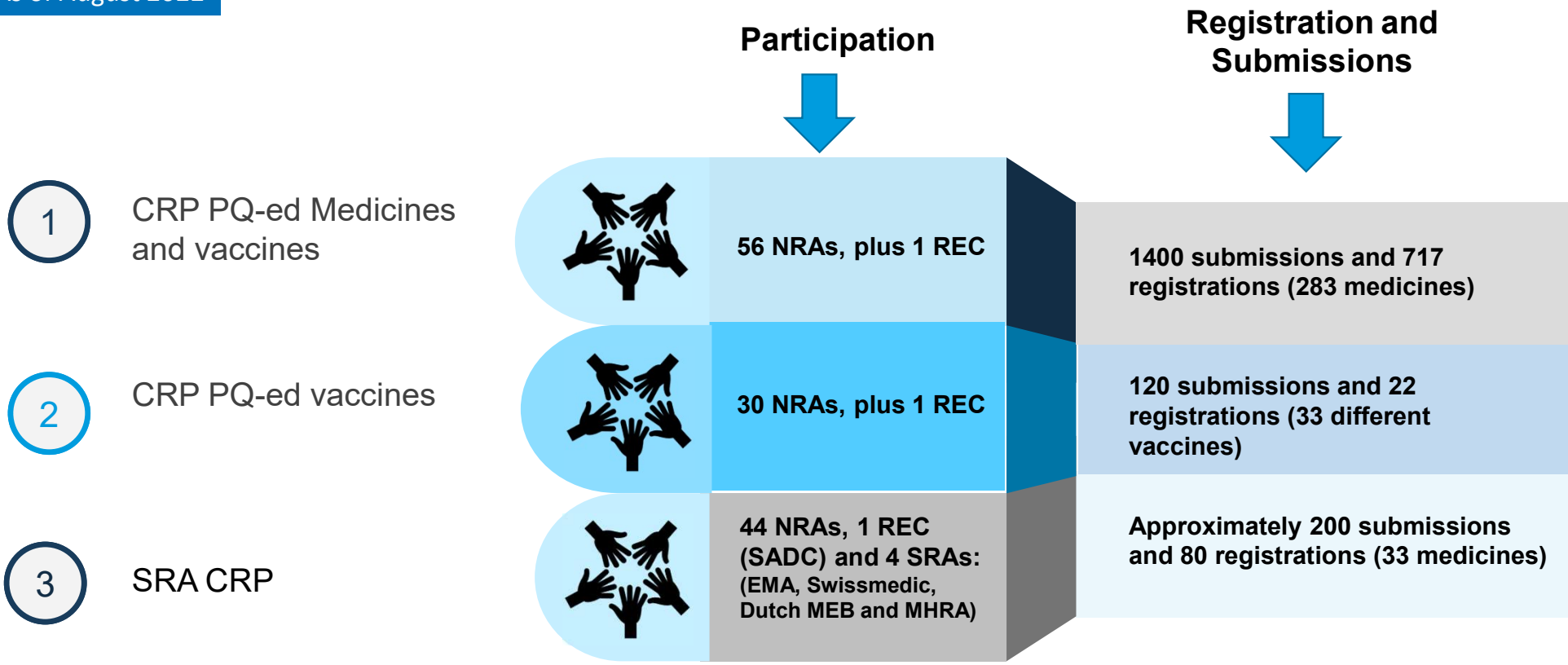
CRP in facilitating in-country regulatory approval of medical products

As of August 2022



Reliance is “implanted” in facilitated regulatory pathways

WHO PQ collaborative registration procedure

- Vaccines: 2004
- Medicines: Started in 2012
- FDA-WHO joint pilot to accelerate access to HIV medicines (CRP-lite)
- 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 regulatory harmonization initiatives and networks

African Medicines Regulatory Harmonization Initiative (AMRH)

ASEAN SIAHR Project

CARPHA

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

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

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WORKING TOGETHER

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

Back-up slides

5A 340-400 million more patients are accessible thanks to resources freed up by PQ

Product stream	Freed up budget[1] USD Mn (% of market[2])	÷	Treatment cost/year USD	=	Additional patients accessible[1], Mn	Methodology
Rx-HIV	147 - 196 28 - 37%		93.35		1.6 - 2.1	▪ Treatment cost per year = Total sales / total # treatments ▪ Most ARVs require daily pills ▪ CHAI estimates 94 USD/year in 2016
Rx-Malaria	124 - 145 39 - 45%		0.68		183 - 213	▪ Based on GF reference treatment pricing for largest product in 2018 ▪ Considered 1 adult dose treatment per year (twice daily for 3 days)
Rx-TB	13 - 19 9 - 14%		662		0.0	▪ Treatment cost per year is weighted average of FLDs and SLDs[3] cost ▪ Based on Global Drug Facility sales in 2017
Rx-RH	0 0		3.60		0	▪ CHAI RH 2018 report for treatment pricing, using market value to determine average cost
Vx	337 - 382 17 - 19%		2.19		154 - 174	▪ # doses for each of top 5 drugs according to WHO recommendation used to determine vaccination cost
Dx	3.4 – 7.7 1 - 3%		1.33		2.5 – 5.8	▪ 1 unit is equal to 1 diagnosis ▪ Considered 1 diagnosis per year ▪ Average price of HIV diagnosis

Assuming a fixed donor market size for all products, calculated the share of the market represented by savings (i.e. the freed up budget). Treatment cost/year price only includes price of the product itself.

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

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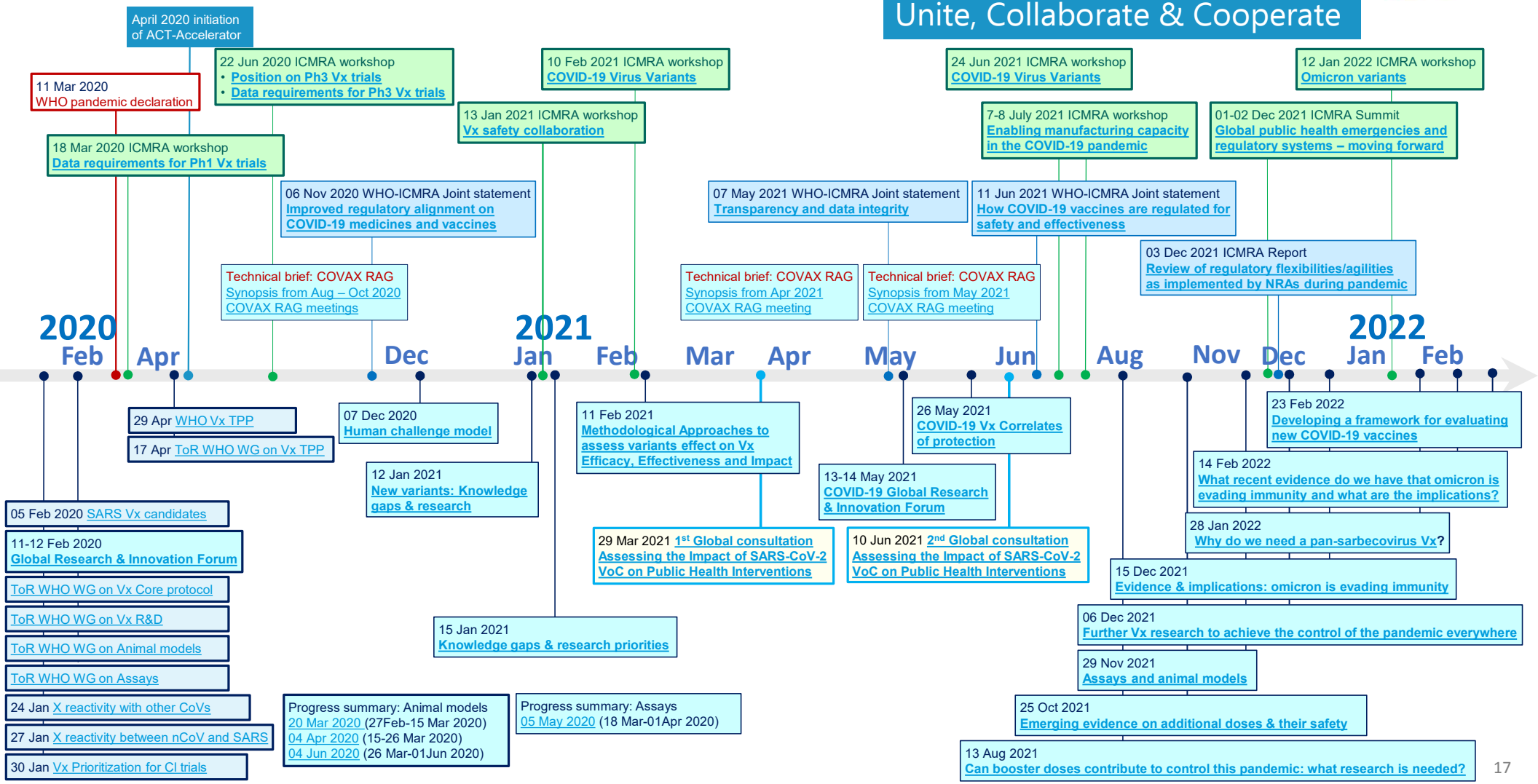
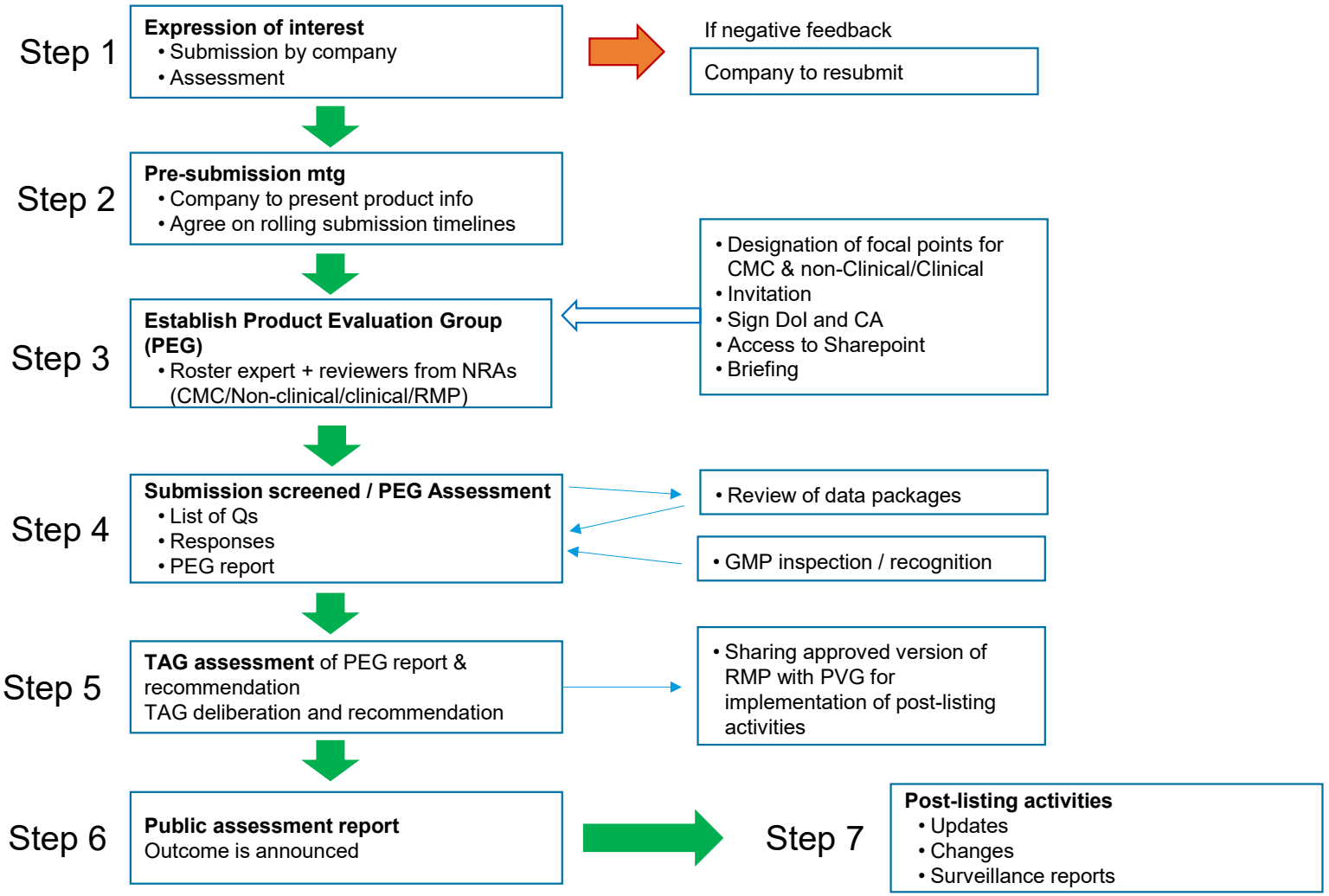
Unite, Collaborate & Cooperate

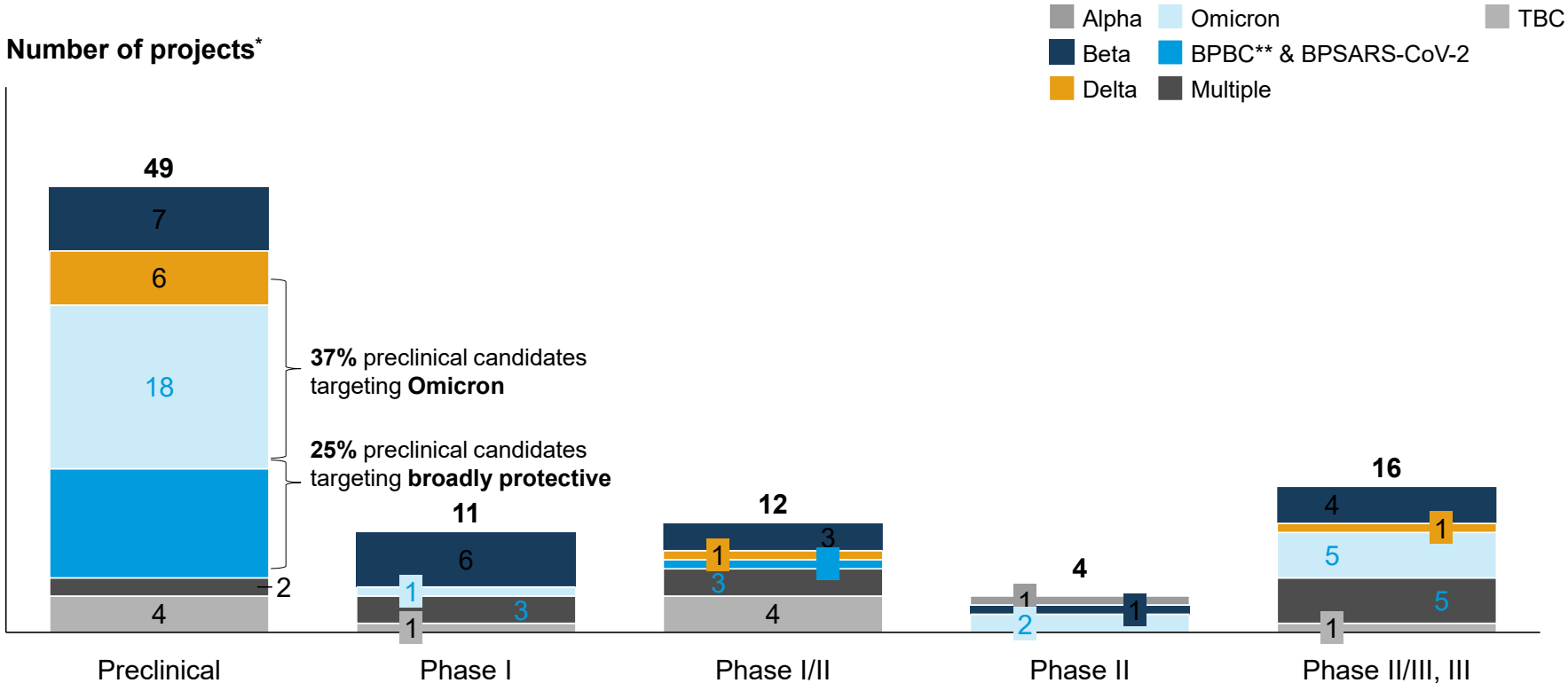


WHO Emergency Use Listing process



Clinical evidence is required for variant vaccines to be authorized and implemented in programmes

COVID-19 current vaccine development pipeline – Variants*



*Adapted from Cepi 5 Aug 22 - Based on publicly available information from vaccine candidates based on variants
**Broadly protective Beta coronavirus

Variant-containing COVID-19 vaccines

As of 31 August 2022

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Manufacturer	Variant-containing vaccine	Publicly available data	
		Animal model data	Clinical data
Moderna	mRNA1274.211 (Beta) monovalent		Yes[1,2]
	mRNA1274.211 (Beta) bivalent		Yes[1,2]
	mRNA1274.214 (Omicron BA.1) bivalent	Yes[3,4]	Yes[5]
	mRNA1274.214 (Omicron BA.5) bivalent	-	-
Pfizer	BNT162b2 (Omicron BA.1) monovalent	Yes[6]	Yes[6]
	BNT162b2 (Omicron BA.1) bivalent	Yes[6]	Yes[6]
	BNT162b2 (Omicron BA.5) bivalent	Yes[6]	-
Sanofi/GSK	Beta monovalent		Yes*
	Beta + D614 bivalent		Yes*

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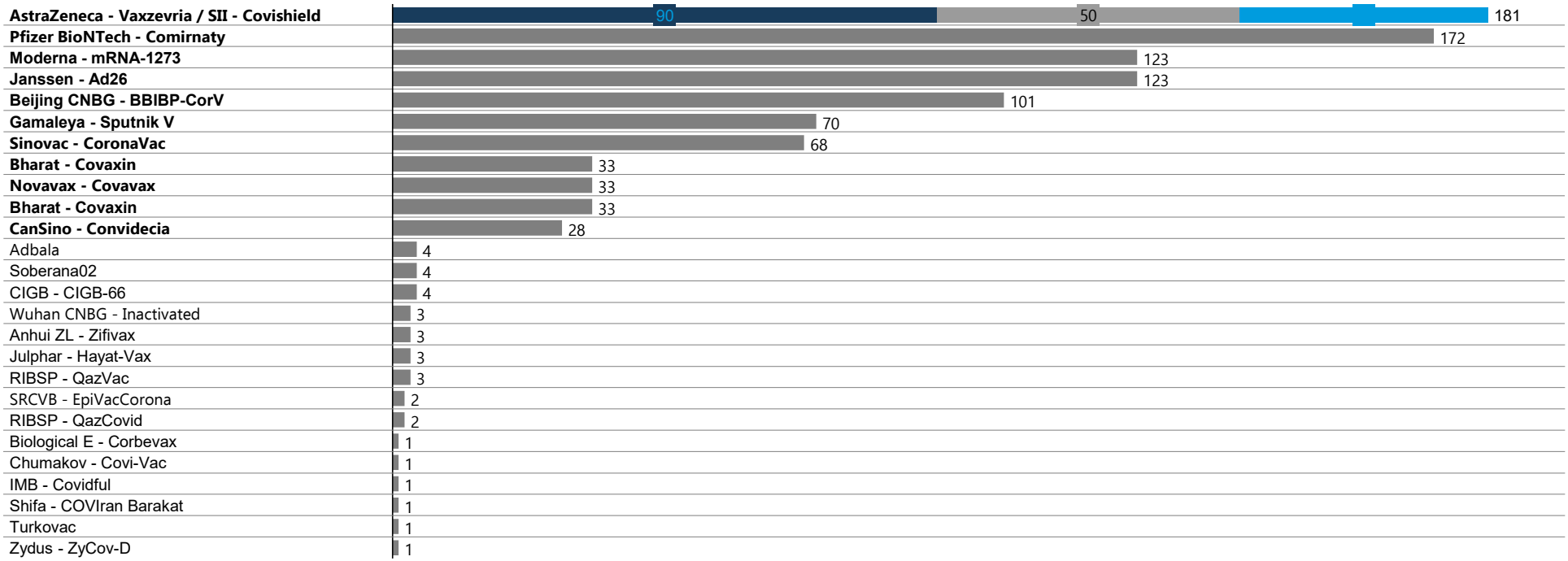
*Shared with WHO; not in public domain
Under development: Novavax Omicron-containing product; Sinopharm Omicron-containing product

Adding variant adapted vaccines to portfolios as boosters potential additional operational complexity for countries

INDICATIVE // NON-EXHAUSTIVE **DATA AS OF AUGUST 15, 2022**

Countries & economies using available vaccines, Cumulative number of different vaccines products used



12 countries and economies are using 1 vaccine; 206 are using 2 or more vaccines[1]

1. World Bank classification (2021) of 218 economies. Note: The term country, used interchangeably with economy, does not imply political independence but refers to any territory for which authorities report separate social or economic statistics.

Source: Our World in data, WHO COVID-19 dashboard, Government websites; Press research