REGIONAL VACCINE REGULATORY LANDSCAPE ANALYSIS AND RECOMMENDATIONS

A REVIEW OF VACCINE REGULATORY ECOSYSTEM ACROSS FIVE COUNTRIES IN ASIA AND THE PACIFIC

Collaboration between

Asian Development Bank (ADB)

and

Centre of Regulatory Excellence (CoRE)

Duke-NUS Medical School, Singapore

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This report is prepared by the Duke-National University of Singapore (NUS) Centre of Regulatory Excellence (CoRE) and commissioned by ADB. It provides a regional assessment of the vaccine ecosystem and regulatory frameworks based on the findings gathered of five countries, namely Bangladesh, India, Indonesia, Republic of Korea and Singapore. Findings were collected from a systematic literature review, structured interviews with key stakeholders and insights garnered from the regional multi-stakeholder ADB-CoRE Vaccine Seminar titled, "Fit-for-Purpose Vaccine Technologies: The Amalgamation of Science, Policy and Practice", held from 5-7 October 2023. Key recommendations on regulatory systems strengthening from this report will help to lay the foundations for building functional national regulatory systems and strengthen regulatory resilience for public health emergencies in Asia and the Pacific, particularly in low-resourced DMCs.

About the ADB-CoRE Vaccine Regulation Project

The ADB-CoRE Vaccine Regulation Project aims to inform the Asian Development Bank (ADB) Health Sector Group on the vaccine regulatory landscape in Asia and the Pacific, focusing on Bangladesh, India, Indonesia, Republic of Korea and Singapore. Sustainable vaccine manufacturing and regulatory systems strengthening in ADB developing member countries (DMCs) are pivotal in encouraging equitable access to innovative health products, attracting investments and enhancing public health resilience in this region.

This project initiated in 2022 has facilitated public-private vaccine stakeholder engagements among ADB developing member countries (DMCs) and produced country-specific and regional landscape analysis reports. Through these activities, the project laid the foundations for developing a strong network of developers, manufacturers and regulators to advance equitable access of innovative therapies among the ADB DMCs.

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Abbreviations

ADB	Asian Development Bank
APEC	Asia-Pacific Economic Cooperation
AHC	APEC Harmonization Center
APVAX	Asia Pacific Vaccine Access Facility
ASEAN	Association of Southeast Asian Nations
ASEAN PPWG	ASEAN Pharmaceutical Product Working Group
AVSSR	ASEAN Vaccine Security and Self-Reliance
GF	Gates Foundation
BPOM	Badan Pengawas Obat dan Makanan, Indonesia
CDSCO	Central Drugs Standard Control Organisation, India
CEPI	Coalition for Epidemic Preparedness Innovation
CoRE	Centre of Regulatory Excellence
CPP	Certificate of Pharmaceutical Product
CTD	Common Technical Document
DBT	Department of Biotechnology, India
DCVMN	Developing Countries Vaccine Manufacturing Network
DGDA	Directorate General of Drug Administration, Bangladesh
DMC	ADB Developing Member Country
EUA	Emergency Use Authorisation
EPI	Expanded Programme for Immunisation
EUL	Emergency Use Listing
FDA	Food and Drug Authority
GBT	Global Benchmarking Tool
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GTH-B	Global Training Hub for Biomanufacturing
HSA	Health Sciences Authority, Singapore
iccdr,b	International Centre for Diarrheal Disease Research (Bangladesh)
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICMRA	International Coalition of Medicines Regulatory Authorities
IDP	Institutional Development Plan
IEDCR	Institute of Epidemiology, Disease Control and Research (Bangladesh)
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
IND	Investigational New Drug
IVI	International Vaccine Institute
KIDS	Korea Institute of Drug Safety and Risk Management
LMIC	Low-to-middle income countries
LR	Lot Release
LT	Laboratory Testing
MC	Market Surveillance and Control
MFDS	Ministry of Food and Drug Safety, Korea
MOH	Ministry of Health
NCL	National Control Laboratory
NDCT	National Drugs and Clinical Trials Rules 2019 (India)
NIP	National Immunisation Programme
NRA	National Regulatory Authority
NVI	National Vaccine Institute

PIC/S	Pharmaceutical Inspection Cooperation Scheme
PQ	WHO Prequalification
PQM+	United States Pharmacopeial Conventions' Promoting Quality of Medicines Programme
R&D	Research and Development
RHSC	APEC Regulatory Harmonization Steering Committee
RIGHT Foundation	Research Investment for Global Health Technology Foundation
RSS	Regulatory systems strengthening
RVMC	Regionalized Vaccine Manufacturing Cooperative
SAARC	South Asian Association for Regional Cooperation
SEARN	WHO South-East Asia Regulatory Network
USAID	United States Agency for International Development
USP	United States Pharmacopeia
WHO	World Health Organization
WLA	WHO-Listed Authority

Definitions

Asia and the Pacific region

Refers to the broad region of countries in Asia and the Pacific that includes Asian Development Bank (ADB) member countries, and World Health Organization (WHO) South-East Asia and Western Pacific sub-regions

Regulatory convergence

The greater *alignment* of regulatory requirements over time, as distinct from "regulatory harmonisation" that refers to the *uniformity* of technical guidelines across participating NRAs[1]

Regulatory reliance

The practice of a relying NRA giving significant weight to the assessments made by a reference agency when making an independent decision[2]

1 Executive Summary

Regulatory systems across Asia and the Pacific are highly diverse, with a wide spectrum of regulatory maturity levels (ML). This poses a challenge to timely and equitable access to vaccines, health products and other medical countermeasures across regional markets, particularly during public health emergencies.

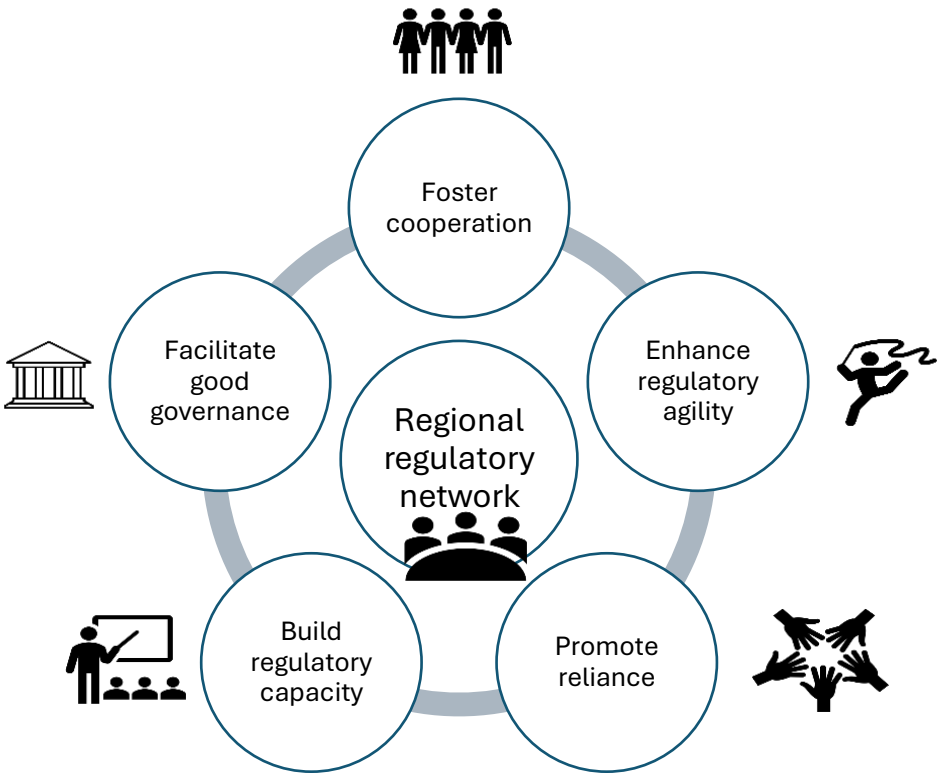
The Asian Development Bank (ADB) commissioned the Duke-NUS Centre of Regulatory Excellence (CoRE) under the Asia Pacific Vaccine Access Facility (APVAX) to conduct a regional regulatory landscape analysis of vaccine manufacturing, with the goal of strengthening regulatory resilience for public health emergencies. Five countries with varying regulatory maturity levels (ML) and state of vaccine manufacturing were selected to be part of the regional vaccine regulatory landscape analysis in the ADB-CoRE Vaccine Regulation Project. The five countries selected are Bangladesh, India, Indonesia, Republic of Korea and Singapore.

This regional landscape analysis report is informed by the data gathered from systematic literature review, expert opinions from semi-structured interviews with key stakeholders and insights garnered from the multi-stakeholder ADB-CoRE Vaccine Seminar on *"Fit-for-Purpose Vaccine Technologies: The Amalgamation of Science, Policy and Practice"* conducted from 5-7 October 2023 at Duke-NUS Medical School in Singapore. Key stakeholders comprised representatives of the five countries, delegated with responsibilities, or possessing established and relevant experience in vaccine regulations or in the vaccine production life cycle. These include individuals involved in government policy, international organisations, regulatory authorities as well as vaccine development and manufacturing.

Analysis of the best practices, challenges and opportunities of the vaccine regulatory landscape within the five selected countries highlight that there is a need to better address the diverse regulatory requirements and varying levels of maturity in national regulatory systems. In addition, maintaining strong regulatory systems and a robust vaccine ecosystem necessary for sustainable vaccine manufacturing to support routine immunisation programmes and in public health emergencies is highly resource intensive. Taking a broader regional and global perspective, the landscape analysis indicates that while support is available to provide the relevant resources needed to strengthen national regulatory systems and facilitate the development of local vaccine production, a more coordinated approach is needed to ensure longer term sustainability.

These findings suggest that to strengthen regulatory systems, particularly for low-resourced developing member countries (DMCs) of the ADB, a whole-of-region approach could potentially enhance the coordination of resource support. This would also better leverage and build on existing international and sub-regional regulatory platforms to facilitate the application of more common and aligned regulatory standards to strengthen regulatory cooperation. A significant strategic step forward would be to form a regional level regulatory network or alliance in Asia and the Pacific. Such a neutral, inclusive and multi-stakeholder regional regulatory alliance would be key to supporting the successful implementation of the five key recommendations in this report to strengthen regulatory systems and enable sustainable vaccine manufacturing. These are (1) fostering cooperation, (2) enhancing regulatory agility, (3) promoting reliance, (4) building regulatory capacity, and (5) facilitating good governance (Figure 1). These are vital for building functional national regulatory systems in DMCs to better support sustainable vaccine manufacturing and strengthen regional regulatory resilience across Asia and the Pacific.

Figure 1: Key recommendations of the regional landscape analysis report



2 Introduction

2.1 Background

The COVID-19 pandemic highlighted significant challenges in timely and equitable access to vaccines and other critical medical countermeasures. Data shows that this disparity in access often leaves lower-resourced countries more vulnerable compared to high-income counterparts. In Asia-Pacific, it is estimated that lower-income countries experienced almost 12% higher mortality from the COVID-19 Omicron variant as compared to higher income countries due to differences in vaccine coverage[3]. One key contributing factor is the predominant concentration of vaccine manufacturing sites in developed countries, which can increase the susceptibility of the global vaccine ecosystem to supply chain disruptions. Attempts at equitable global distribution such as the COVAX initiative were only moderately successful, delivering less than half of the two billion doses originally projected and representing only a portion of the over 9 billion doses administered worldwide for 2021[4].

One way to more effectively address this is diversifying vaccine manufacturing in low-resourced countries. However, regulatory challenges have been recognised as one of the most critical barriers to sustainable vaccine manufacturing[5, 6]. The World Health Organization (WHO) estimates that only 30% of national regulatory authorities (NRAs) possess the capacity to regulate health products effectively[7]. Among the member states of the Association of Southeast Asian Nations (ASEAN), only four out of the ten member states had attained well-functioning regulatory capacity as of June 2024[8]. Strong regulatory systems ensure the production of good quality, efficacious and safe vaccines for local, regional and global markets. With vaccine research and development (R&D) being integral to sustainable vaccine development and production, good regulation serves as a key enabler to facilitate and guide the advancement of science and innovation[9].

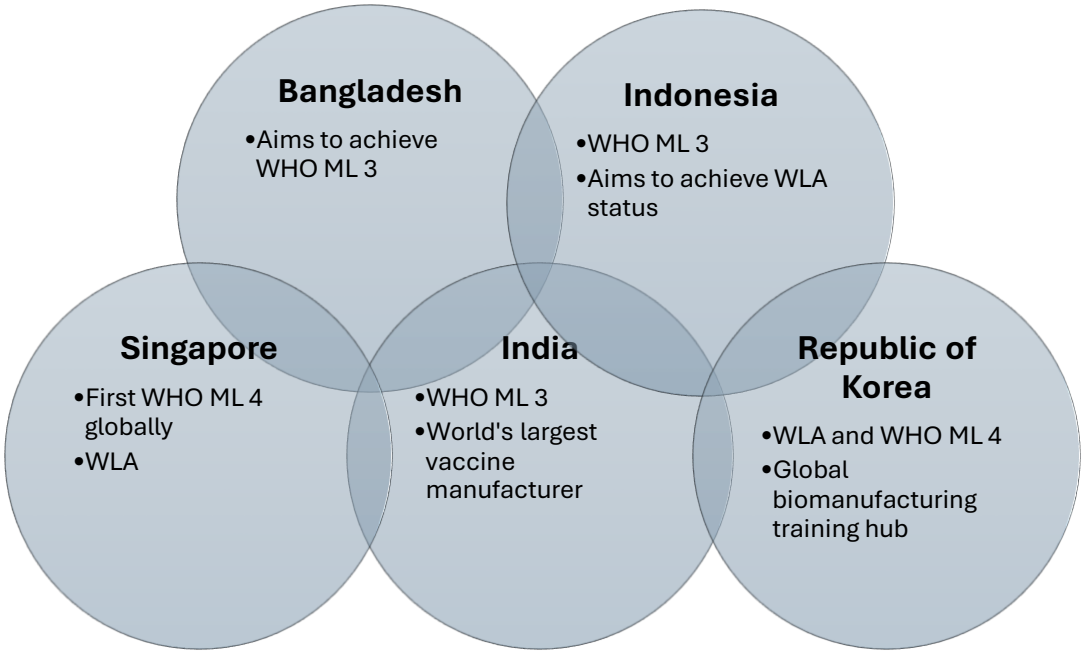
2.2 About the Project

In response to these needs, the Health Sector Group of the Asian Development Bank (ADB) has collaborated with the Centre of Regulatory Excellence (CoRE) under the Asia Pacific Vaccine Access Facility (APVAX) programme to strengthen regulatory resilience for public health emergencies. The ADB-CoRE Vaccine Regulation Project aims to inform the Health Sector Group of ADB on the vaccine regulatory landscape in Asia and the Pacific, focusing on

Bangladesh, India, Indonesia, Republic of Korea and Singapore. The strengthening of regulatory systems is key to supporting sustainable vaccine manufacturing, enhancing the region's resilience against public health emergencies.

The five countries were selected based on their different regulatory maturity levels (ML) and state of vaccine manufacturing to characterise the regulatory factors needed for sustainable vaccine manufacturing (Figure 2). The diverse range of maturity in regulatory systems and vaccine manufacturing among the selected countries can provide a unique vantage point from which ADB and other DMCs in Asia and the Pacific can better understand the regulatory challenges and opportunities to support regionalisation of vaccine production. Bangladesh aims to achieve a functional national regulatory system of WHO ML 3. Indonesia, which has a regulatory system of WHO ML 3, aims to achieve WHO-Listed Authority (WLA) status. India is the world's largest vaccine manufacturer with a functional regulatory system of WHO ML 3. The Republic of Korea is designated by WHO as the global training hub for biomanufacturing[10]. For its advanced regulatory system, it has also achieved the highest classification of regulatory maturity WHO ML 4 status as a medicines and vaccines producing country. Singapore was the first NRA in the world to achieve WHO ML 4 status for medicines[11]. Both the Republic of Korea and Singapore were among the first three countries to be recognised as attaining WLA status in October 2023 (together with Switzerland)[12].

Figure 2: Overview of the five countries selected under this project



This project is focused on reviewing the vaccine regulation in these five countries involving vaccine life cycle stages of research and development (R&D), clinical trials, market authorisation, manufacturing, licensure, inspections, post-approval changes and pharmacovigilance. Data was gathered from a systematic literature review, expert opinions from semi-structured interviews with key stakeholders, and insights garnered from the multi-stakeholder ADB-CoRE Vaccine Seminar on *"Fit-for-Purpose Vaccine Technologies: The Amalgamation of Science, Policy and Practice"* conducted from 5-7 October 2023 at Duke-NUS Medical School in Singapore. The key stakeholders selected are those delegated with responsibilities or possessing established and relevant experience in vaccine regulation or in the vaccine production life cycle in the five countries. These include individuals involved in government policy, international organisations, regulatory authorities as well as vaccine development and manufacturing.

2.3 Relevance and Impact of the Regional Landscape Analysis Report

This regional landscape analysis report provides an assessment of the unique opportunities and challenges of the NRAs of these five selected countries for regulatory systems strengthening. It aims to inform on the regulatory factors needed to support sustainable vaccine manufacturing, particularly for lower-resourced ADB DMCs.

Aligning with the growing global interest in adopting a regional approach to sustainable vaccine production, this regional report also aims to provide ADB with regional level recommendations for Asia and the Pacific that are set within the global context, to address the short and long-term investments required for proposing the way forward. Notably, the World Economic Forum (WEF) has advocated regionalisation to ensure greater resilience, responsiveness and equity in meeting region-specific vaccine needs, and has correspondingly established the Regionalized Vaccine Manufacturing Cooperative (RVMC)[13]. RVMC estimates that the socioeconomic returns from investing in regional vaccine manufacturing systems would likely exceed that of investing solely in a national model within a short period of five years[14]. Thus, recommendations from this report can contribute to supporting regulatory capacity building and regulatory systems strengthening at a regional level, particularly to benefit other DMCs in Asia and the Pacific in promoting regulatory resilience for managing public health emergencies.

3 Vaccine Ecosystem of the Five Countries

3.1 Background of the Regional Vaccine Ecosystem

There is a dynamic vaccine ecosystem in Asia and the Pacific, with the regional market projected to continue to expand in the short to medium term. It has been estimated that the preventive vaccines market in the Asia-Pacific will grow from 2023 at a compound annual growth rate of about 13% from US$20.9 billion in 2023 to over US$63 billion by 2032[15]. This region is also home to over 60% of the world's population, including the world's most populous countries of India and China[16]. Globally, India is a vaccine manufacturing powerhouse, producing more than 60% of the world's vaccines by volume prior to the COVID-19 pandemic[17]. The region also has the greatest share of global R&D, including substantial publications and patents on vaccine R&D[18].

At the same time, many countries in this region, particularly those in South Asia, are among those with the highest proportions of global burden of disease from infectious diseases[19], with highly dense urban populations and their tropical or subtropical climates contributing to a favourable environment for disease transmission and a higher disease burden. Vaccine production is primarily concentrated in high income countries to reap economies of scale[13]. However, this increases susceptibility to supply chain disruptions that are more likely to be exacerbated during public health emergencies when low-resourced DMCs are particularly vulnerable to lack of supply. Thus, diversifying vaccine manufacturing for lower-resourced countries would help to address this public health challenge and improve health outcomes against vaccine-preventable diseases. It should also be noted that investing in sustainable local vaccine manufacturing in Asia and the Pacific is key not only for managing pandemic prevention, preparedness and response, but also to support national immunisation programmes (NIP) for routine immunisation in peacetime.

3.2 Local Stakeholders of the National Vaccine Ecosystems in the Five Countries

Sustainable local vaccine manufacturing encompasses an inclusive end-to-end approach, engaging all stakeholders along the entire vaccine lifecycle. Mapping of relevant stakeholders across the vaccine ecosystem is important for countries that are building up local vaccine manufacturing capabilities, particularly for low-resourced DMCs transitioning out of Gavi support, such as Bangladesh by 2029 (Table 1). In 2020, Gavi provided more than 60% of the

funds needed to support Bangladesh's Expanded Programme for Immunisation (EPI)[20]. This means countries like Bangladesh will need to boost their ability to self-finance vaccines under the NIP, which sustainable local and regional vaccine production coupled with a good understanding of the relevant stakeholders in the ecosystem will be pivotal in supporting. An important reference point for low-resourced DMCs transitioning out of Gavi would be understanding how vaccine stakeholders are organised in the ecosystem of countries that have recently transited out of Gavi, such as Indonesia which transited out of Gavi in 2017 and is fully self-financing all vaccines under its NIP.

Table 1 outlines the key stakeholders of the vaccine ecosystem from government agencies and affiliated organisations, NRAs, industry and associations, academia and others. Detailed descriptions of stakeholders of the five countries can be found in Annex I, along with an overview of the vaccine and regulatory ecosystems of the five countries in Annex II. Of note, the COVID-19 pandemic catalysed governments to establish initiatives to better coordinate efforts between key stakeholders in domestic vaccine R&D and manufacturing to enable rapid vaccine development and boost national vaccine resilience. Examples include Indonesia's Vaccine Collaborating Centre (VOLARE) initiative, Republic of Korea's Vaccine Innovative Technology Alliance Korea (VITAL-Korea) and Singapore's Programme for Research in Epidemic Preparedness and Response (PREPARE).

Table 1: Key stakeholders of the vaccine ecosystem from government agencies, NRAs, industry and associations, academia and others

Government Agencies and Affiliated Organisations	NRA	Industry and Associations	Academia and Others
Bangladesh			
• Bangladesh Medical Research Council (BMRC) • Institute of Epidemiology, Disease Control and Research (IEDCR) • Institute of Public Health (IPH) • Ministry of Health and Family Welfare (MOHFW)	Directorate General of Drug Administration (DGDA)	• Active Fine Chemicals Ltd* • Bangladesh Association of Pharmaceutical Industries (BAPI) • Essential Drugs Company Ltd* • Globe Biotech Ltd* • Healthcare Pharmaceuticals Ltd • Incepta Pharmaceuticals Ltd • Popular Pharmaceuticals Ltd *developing vaccine manufacturing capabilities	• Bangabandhu Sheikh Mujib Medical University • Dhaka Medical College • Child Health Research Foundation • International Centre for Diarrheal Disease Research (iccdr,b)
India			
• Biotechnology Industry Research Assistance Council (BIRAC)* • Central Drugs Laboratory (Kasauli)	• Central Drugs Standard Control Organisation (CDSCO)	• Bharat Biotech International Ltd • Biological E. Ltd • Cadila Pharmaceuticals Ltd • Gennova Biopharmaceuticals Ltd	• Central Research Institute, Kasauli • Haffkine Institute for Training, Research and Testing

• Genetic Engineering Approval Committee (GEAC)* • Indian Council of Medical Research (ICMR) • India Department of Biotechnology (DBT) • National Board for Accreditation of Testing and Calibration Laboratories (NABL) • Review Committee on Genetic Manipulation (RCGM)* *DBT-affiliated		• Organisation of Pharmaceutical Producers of India (OPPI) • Panacea Biotec Ltd • Pasteur Institute of India • Serum Institute of India Ltd • Shantha Biotechnics • Techinvention Lifecare Pvt. Ltd • Zydus Lifesciences Ltd	• National Institute of Pharmaceutical Education and Research (NIPER) • Translational Health Science and Technology Institute (THSTI)
Indonesia			
• Forum for Ethical Review Committees in Asia and the Pacific (FERCAP) • Indonesian Clinical Research Centre (INA-CRC) • Indonesian National Health Research and Development	Indonesian Food and Drug Authority (FDA), also known as Badan Pengawas Obat dan Makanan or BPOM	• PT Bio Farma • PT. Biotis Pharmaceutical Indonesia • PT Etana Biotechnologies Indonesia • PT Jakarta Biopharmaceutical Industry (JBio)	• Airlangga University • Bandung Institute of Technology (ITB) • BRIN Research Center for Molecular Biology (formally Eijkman Institute) • Gadjah Mada University • University of Indonesia

Ethics Committee (KEPPKN) Indonesian Ministry of Health • National Research and Innovation Agency (BRIN)			
Republic of Korea			
• Korea Advanced Center for Vaccine Development (KAVAD) • Korea Disease Control and Prevention Agency (KDCA) • Korea Institute of Drug Safety and Risk Management (KIDS)* • National Institute of Food and Safety Evaluation (NIFDS)*[21] • Korea National Enterprise for Clinical Trials Korea (KoNECT) • Regulatory Research Center (K-RSC) • Ministry of Health and Welfare (MOHW)	• Ministry of Food and Drug Safety (MFDS)	• CHA Vaccine Institute • CJ Healthcare • EuBiologics, Co., Ltd • GC Pharma • GeneOne Life Science • Korea Biomedicine Industry Association (KoBIA) • InThera • LG Life Sciences Ltd • SML Biopharm • SK Bioscience Co., Ltd	• Andong National University • International Vaccine Institute (IVI) • Seoul National University

• Vaccine Innovative Technology ALliance Korea (VITAL-Korea) *MFDS-affiliated			
Singapore			
• Agency for Science, Technology and Research (A*STAR)** • Consortium for Clinical Research and Innovation, Singapore (CRIS) • Economic Development Board (EDB) • National Centre for Infectious Diseases (NCID) • National Medical Research Council (NMRC) • Programme for Research in Epidemic Preparedness and Response (PREPARE)* • Singapore Ministry of Health (MOH) *National programme by MOH and hosted by NCID	Health Sciences Authority (HSA)	• BioNTech Pharmaceuticals Pte Ltd**[22] • CoV Biotechnology • GlaxoSmithKline Biologicals (production in 2027)**[23] • Hilleman Laboratories [24] • MSD[25] • Sanofi Manufacturing Pte Ltd**[26] • Thermo Fisher Scientific [27] **Part of Biologics Pharma Innovation Programme Singapore (BioPIPS) Consortiu	• Duke-NUS Medical School • National Technology University (NTU)** • National University of Singapore (NUS)** • Singapore Institute of Technology (SIT)** • Singapore Clinical Research Institute (SCRI)

4 Regulatory Systems of the Five Countries

Regulation is a key enabler and an integral part of the global vaccine ecosystem. It enables access to safe, efficacious and quality vaccines in a timely manner and has proven critical during public health emergencies such as the COVID-19 and more recent mpox pandemics. In addition, a strong national regulatory system is essential to the economic sustainability of local vaccine production by enabling access to global markets. Vaccines that are produced in a country where the NRA is performing at least at WHO ML 3 are eligible to be considered under the WHO prequalification programme, where vaccines can be purchased by global procurement agencies such as Gavi and UNICEF.

With the ambit to support NRAs to strengthen regulatory systems in accordance with Resolution WHA 67.20, the WHO regulatory systems strengthening (RSS) programme has developed an assessment tool, the WHO Global Benchmarking Tool (GBT). This framework evaluates the performance and maturity levels of NRAs, where NRAs with "functional" regulatory systems are designated as WHO ML 3 and regulatory systems performing at the highest level are designated as WHO ML 4. WHO estimates that only 30% of the NRAs globally have achieved at least a functional level of regulatory oversight at ML 3[7]. This framework also recognises NRAs performing at the highest regulatory level and capabilities as WLAs, potentially serving as reference agencies for other lower-resourced NRAs[28]. The WHO GBT and benchmarking support NRAs in regulatory systems strengthening through the co-creation of an Institutional Development Plan (IDP), taking into consideration the strengths and areas for improvement.

4.1 Overview of the National Regulatory Systems of the Five Countries

The regulatory systems in Asia and the Pacific are diverse, as evident in the five countries selected for this project. Table 2 lists the five countries against the WHO GBT benchmarking and those designated as WLAs as of June 2024[8, 29]. Details of the regulatory systems of the five countries can be found in Annex II.

Table 2: Countries benchmarked as ML3 and ML4 using the WHO GBT and recognised as WLAs

Country	NRA	ML	Scope of Products	WLA Status	Year Announced
Bangladesh	DGDA	*Not listed*			
India	CDSCO	ML 3	Vaccines (producing)	*Not listed*	2017
Indonesia	Indonesian FDA	ML 3	Vaccines (producing)	*Not listed*	2019
Republic of Korea	MFDS	ML 4	Medicines Vaccines (producing)	Medicines Vaccines	2022 (ML4) 2023 (WLA)
Singapore	HSA	ML 4	Medicines Vaccines (non-producing)	Medicines	2022 (ML4) 2023 (WLA)

4.2 Regulatory Landscape by Stages of the Vaccine Life Cycle

Table 3 shows an overview of the regulatory landscape of the five countries, organised into different stages along the vaccine life cycle. The regulatory best practices among the five countries can be distilled into the 3 key regulatory factors discussed below for maturing NRAs of lower-resourced countries to consider for the strengthening of national regulatory systems.

Regulatory Best Practice: Practise Reliance

- Reference the regulatory assessments made by established and mature regulatory agencies in regulatory decision making. List of reference agencies can be expanded to include other well-functioning mature regulatory agencies.
- Learning from the best practices practised at various stages along the vaccine life cycle. These include leveraging the regulatory assessments of reference agencies for facilitated abridged pathways, inspections that use harmonised Good Manufacturing Practice (GMP) standards, for post-market variation approvals and lot release testing.
- Build consensus among NRAs on the minimum information required in public assessment reports [30]

Regulatory Best Practice: Adopt Regulatory Convergence and Harmonisation

- Participate in international entities, which can provide significant impetus for harmonisation and convergence, for example the Pharmaceutical Inspection Cooperation Scheme (PIC/S) for GMP inspections
- Adopt harmonised guidelines in regulatory requirements such as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) on the Common Technical Document (CTD) and PIC/S on GMP requirements
- Adopt consistent product variation classification, including with reference to the WHO guidelines Annex 4 TRS No 993. This can facilitate reliance-based abridged pathways for post-approval changes

Regulatory Best Practice: Enhance Agility

- Streamlining of the regulatory framework, where fit-for-purpose regulation reduces administrative burden and can facilitate regulatory resilience to enable NRAs to respond more effectively in public health emergencies. Examples of the various forms of streamlining at different stages of the vaccine life cycle are as follows:
    - R&D: streamlining the number of government entities needed to grant regulatory approval
    - Clinical trials: waiver of requirement for local clinical trials, such as the recently implemented local clinical trial waiver in India for health products like vaccines and drugs used in pandemics
    - Licensure: streamlining and reduction of administrative procedures such as not mandating the need for a certificate of pharmaceutical product (CPP), both in guidelines and in practice
    - Licensure: Availability of risk-based accelerated market authorisation pathways for vaccines and other critical health products for public health emergencies
    - Licensure: Availability and accessibility to pre-submission consultation, particularly at the early stage of vaccines product development, supported by provision of product-specific regulatory guidance
    - Manufacturing: Including multiple manufacturing sites under a single licence, which enables flexibility to scale up production for manufacturers while reducing regulatory burden of multiple submissions for each site
    - Inspections: recognition of GMP certificates issued by exporting countries. Of note, mutual recognition agreements for GMP certificates issued by PIC/S

member countries minimise the need for inspections at foreign manufacturing sites

- Lot release: recognition of lot release certificates by the importing country not only for prequalified vaccines, but also for vaccines where the lot release certificates are issued by exporting countries that have attained “functional” regulatory maturity
- Pharmacovigilance: Leverage digitalisation for the national pharmacovigilance (PV) network to augment PV surveillance

Table 3: Overview of the regulatory landscape of the five focus countries by stages of the vaccine life cycle

Life cycle stage	Bangladesh	India	Indonesia	Republic of Korea	Singapore
WHO maturity level *(as of June 2024)*	Not listed	ML 3	ML 3	ML 4	ML 4
Overall					
Reference agencies	Bangladesh National Drug Policy 2016 lists: - Australia - European Medicines Agency (EMA) - France - Germany - Japan - Switzerland - United Kingdom (UK) - United States (US)	Since August 2024, waiver of requirement for clinical trials in India, if drugs including vaccines and those used in pandemics have been approved in [31]: - Australia - Canada - European Union (EU) - Japan - UK - US	Regulation of the Indonesian Food and Drug Authority Number 15 of 2019 lists: - Australia - Canada - EU - Japan - UK - US	No reference agencies specified.	Listed on HSA's website - Australia - Canada - EU - Switzerland - UK - US
Affiliations/Membership					
APEC Regulatory Harmonization Steering Committee (RHSC)	Not listed	Not listed	APEC RHSC member	APEC RHSC member	APEC RHSC member
International Coalition of Medicines Regulatory Authorities (ICMRA)	Not listed	ICMRA member	Not listed	ICMRA member	ICMRA member
ICH	Not listed	ICH observer	ICH observer	ICH Regulatory Member and member of Management Committee in 2018. MFDS was engaged in 16	Regulatory member of ICH. Served in ICH Management Committee from

				areas of the 34 ICH Working Groups.	June 2018 to June 2021.
PIC/S	Applied for PIC/S pre-accession in 2019 [32].	Not listed	PIC/S member	PIC/S member	PIC/S member
WHO South-East Asia Regulatory Network (SEARN)	SEARN member	SEARN member	SEARN member	WHO Western Pacific Region	WHO Western Pacific Region
R&D					
Pre-submission consultation and other regulatory oversight	-	Regulatory oversight by the DBT. Under DBT, RCGM, GEAC and Institutional Biosafety Committees (IBSC) each have specific functions/requirements, in addition to CDSCO's regulatory requirements. Provision for pre-submission meetings under the New Drugs and Clinical Trials (NDCT) Rules 2019 for licensure, manufacturing or clinical trials.	Pre-submission consultation available, including at pre-IND stage.	In 2020 MFDS formally established "pre-submission consultation division" that primarily provides consultation on clinical trial protocol and approval of products under expedited review[38].	Formal pre-submission consultation available with clarity on requirements[39]. Dedicated Innovation Office provides regulatory support for product innovators.
Clinical Trials					
Clinical trial application (CTA) framework and timeline	Sequential regulatory review by DGDA and ethics review by BMRC[40].	Parallel reviews by CDSCO and institutional ethics committee. Trials are registered with Clinical Trials Registry –	Trials are registered with Indonesia Clinical Research Registry (INA-CRR).	Parallel review of CTA by MFDS and ethics review by institutional review board (IRB). Trials	Parallel review of CTA by HSA and ethics review by IRB. Clear approval timeline of 30 days.

		India (CTRI). Clearly stated approval timelines of 90 days for drugs developed overseas versus 30 days to prioritise locally developed drugs.		are registered with Clinical Research Information Service.	
Market Authorisation					
Certificate of Pharmaceutical Product (CPP)[33, 34]	CPP is required for product registration[35, 36]	Uses CPP or GMP certificate for waiver of foreign manufacturing site inspection. Although guidelines state CPP is not mandatory, it is required in practice[37].	CPP is a routine part of product registration	Waiver of CPP requirement	Accepts but does not require CPP
Facilitated reliance pathways	Adopts reliance practice using the reference agencies as stated above.	In 2006 a two-track system was adopted[41]: - Category A: drugs already approved by stringent NRAs can be approved within 2-4 weeks - Category B: approved within 12 weeks	Adopts facilitated pathway when health product has been approved by ≥1 reference agency, with an abbreviated regulatory timeline of 120 days, as compared to 300 days for the full evaluation route and submission requirements	Does not adopt system using reference agencies for market authorisation.	Facilitated pathways have abbreviated regulatory timelines and submission requirements. - New Drug Application (NDA): 270 working days for full evaluation. - Abridged Route (prior approval by ⩾1 reference agency): 180 working days for

					abridged evaluation. - Verification Route (approved by ≥2 reference agencies): 60 days for verification evaluation.
Accelerated pathways for public health emergencies	Adopts reliance pathway for emergency use authorisation (EUA) of COVID-19 Vaccines.	NDCT Rules 2019 allows for flexibility of data requirements under special circumstances [42]. Adopts reliance pathway for EUA of COVID-19 vaccines. Reference agencies included EU, Japan, UK, US and WHO EUL[43].	Regulation No. 13 of 2021 amendment provides the criteria and requirements of EUA[44].	Global innovative products on fast track (GIFT) provides a pathway to expedite review of innovative products intended for life-threatening or serious diseases such as during public health emergencies, reducing this to 75% of usual review time.	Pandemic Special Access Route (PSAR*): interim authorisation with data submitted on 'rolling' basis for critical novel products. *This route has been mothballed for future use when the COVID-19 situation stabilised to endemic status.
ICH CTD	-	Adopts ICH CTD format.	Accepts both ASEAN CTD and ICH CTD.	Adopts ICH CTD format.	Accepts both ASEAN CTD and ICH CTD.
Manufacturing					
Good manufacturing practice (GMP)	WHO GMP requirements	WHO GMP requirements	WHO, PIC/S GMP requirements[45]	PIC/S GMP requirements. Mutual recognition agreements including with HSA	PIC/S GMP requirements. Mutual recognition agreement between

				and Swissmedic on GMP certification.	HSA and MFDS on GMP certification.
Multiple manufacturing sites under one license[34]	-	-	Practices single license for multiple manufacturing sites.	Practices single license for multiple manufacturing sites.	Practices single license for multiple manufacturing sites.
Pharmacovigilance					
National pharmacovigilance framework - National and global PV network - Active surveillance mechanism - Leverage digitalisation	National Pharmacovigilance Guideline has been incorporated into the Drugs and Cosmetics Act 2023[46]. DGDA is the National Pharmacovigilance Centre of Bangladesh.	The pharmacovigilance Programme of India (PvPI) comprise the National Coordinating Centre (NCC) and over 800 adverse drug monitoring centres. NCC was designated as the WHO Collaborating Centre for Pharmacovigilance in Public Health Programmes and Regulatory Services in 2017[47]. Valid individual case study reports are relayed to the Uppsala Monitoring Centre.	Leveraging on digitalisation, SATUSEHAT is a digital platform of Indonesia and was used for real-time monitoring of COVID-19 vaccines during the pandemic.	National pharmacovigilance network, led by KIDS and comprising 27 regional pharmacovigilance centres (RPVC).	KK Women's and Children's Hospital is designated as the active sentinel surveillance site for adverse events following immunisation (AEFI). HSA leverages electronic health records and data analytics for early detection.
Post Approval Variation					
Guidance, classification of variation and presence of clear implementation timeline	References WHO guidelines Annex 4 TRS No 993.	References WHO guidelines Annex 4 TRS No 993. Released draft guidance document on post approval changes in biological products in Feb 2024[48], which provides clarity and	References WHO guidelines Annex 4 TRS No 993. Clear turnaround time based on classification of variation.	References WHO guidelines Annex 4 TRS No 993. For SARS-CoV-2 vaccine strain update, regarded as new product and	Clear guidance on post-approval process, classification of variation, turnaround time and timeline for implementation.

		addresses previous gaps on classification of variation including on cell bank changes previously highlighted by stakeholders.		stakeholders stated this requires an efficacy study.	Adopts facilitated reliance pathways for variations.
Testing and Lot Release					
- Reliance practice - Affiliations to international networks for sharing of best practices and standardisation of testing - National Control Laboratory (NCL) infrastructure	DGDA is a member of the WHO National Control Labs Network for Biologicals. Guideline on lot release testing available[49]. iccdr,b is in CEPI's Centralised Laboratory Network (CLN)[50].	ICMR and THSTI are members of Coalition for Epidemic Preparedness Innovation's (CEPI) Centralised Laboratory Network (CLN).	Indonesia's NCL is listed as a WHO contract laboratory for vaccine potency testing[51]. BPOM practices some reliance on lot release testing, recognising vaccines certified by stringent NRAs or for WHO prequalified vaccines. However, it conducts testing of other imported vaccines.	NIFDS is a WHO Collaborating Centre for Standardization and Evaluation for Biologicals. It has conducted training and hosted meetings on vaccine testing to facilitate RSS and collaboration[52].	To support Singapore's recent vaccine production, the NCL Biologics Laboratory was established in May 2023. HSA became an associate member of the WHO National Control Labs Network for Biologicals in September 2021. HSA recognises lot release information certified from country of origin without the need to for further lot release testing[53].

5 Challenges and Opportunities from a Regional Perspective on the Vaccine and Regulatory Ecosystem

5.1 The Diverse Regional Regulatory Ecosystem

The wide spectrum in the maturity level of the national regulatory systems and variations in vaccine regulations among the five countries profiled reflect the diversity of national regulatory systems within this region. Diverse regulatory systems and requirements can pose a challenge to vaccine developers to access markets in a timely manner. These challenges can arise from the different formats for submission of market authorisation and post-approval changes and differences in regulatory timelines. For regulators, the challenge of limited transparency of regulatory requirements and information available in public assessment reports can hinder the wider adoption of reliance among NRAs in this diverse regional regulatory ecosystem.

With Asia and the Pacific being home to over 60% of the world's population and the region's growing share of the global vaccine market by volume, it is imperative that the regional vaccine ecosystem is supported by the strengthening of national regulatory systems. This presents an opportunity to better address the diverse regulatory systems across Asia and the Pacific, to facilitate the timely and equitable access of not only vaccines but also health products and medical countermeasures across the region, particularly during public health emergencies.

A short-term fix during the COVID-19 pandemic was the Regulatory Advisory Group (RAG). RAG was formed during the pandemic in 2020 within the COVAX initiative with the intent of expediting regulatory approvals of COVID-19 vaccines, helping vaccine developers work with the diverse regulatory requirements for prompt market access[41]. Although RAG provided vaccine developers with key recommendations on general regulatory filing strategies, its ability to address the diverse regulatory systems and requirements was limited with focus on only COVID-19 vaccines.[54].

In the longer term, it is helpful for the work on driving regulatory convergence and harmonisation to continue. International regulatory entities that help establish or facilitate the adoption of internationally recognised and regulatory standards have been pivotal in promoting regulatory convergence. This helps provide a common ground from which to foster regulatory cooperation and can better support the strengthening of national regulatory

systems. Members of the International Coalition of Medicines Regulatory Authorities (ICMRA), a global network formally established in 2012, consists of NRAs that include Singapore, Republic of Korea and India. Members of ICMRA demonstrated effective regulatory coordination, jointly providing a consensus and direction around innovative strategies to ascertain effectiveness of COVID-19 vaccine boosters in 2021 at a critical time during the pandemic[9]. It has been shown that participation in international regulatory platforms like ICMRA, ICH, PIC/S and others, can support the building of trust and regulatory cooperation, and facilitate regulatory convergence and harmonisation towards internationally recognised standards[34]. Lower-resourced NRAs can also benefit from the access to training resources through these platforms to support the strengthening of national regulatory systems, such as the training provided by PIC/S on GMP inspection for national regulators.

5.2 Supporting the Resource-Intensive Nature of Maintaining Strong Regulatory Systems and Vaccine Ecosystem

Achieving and subsequently maintaining strong regulatory systems can be resource-intensive, particularly for maturing NRAs of low-resourced DMCs. At the same time, vaccine production is highly complex and costly. Upfront investment to establish a new production facility alone can exceed US$100 million[55]. Vaccine candidates also undergo what is often known as the "valley of death" during the development process, making it crucial to de-risk vaccine development[56]. Thus, regional and global partners play a significant role in the provision of technical support and funding assistance.

Providing resources for regulatory capacity building to develop local vaccine production in a coordinated manner among local and global partners is important, particularly to support countries such as Bangladesh transitioning out of Gavi support. For example, WHO established a system of assistance via a Coalition of Interested Parties (CIP), to coordinate and consolidate efforts among an international network of voluntary partners for regulatory systems strengthening in developing countries. For Bangladesh, this provided the necessary resources to support DGDA's efforts in strengthening the National Control Laboratory (NCL) and helps address the targeted aspect of lot release testing identified in Bangladesh's IDP to advance towards achieving ML 3 status[20, 57].

Another example of a coordinated approach among international and regional partners is the Global Training Hub in Biomanufacturing (GTH-B). Jointly organised by the WHO,

International Vaccine Institute (IVI) and the Republic of Korea, manufacturers from lower-resourced DMCs have received training on vaccines and biologics, with the support from ADB to build capacity on vaccine manufacturing [58].

In providing coordinated resource support to build vaccine capacity in low-to-middle income countries (LMICs), one could consider adopting an end-to-end approach to help de-risk vaccine development, where risks tend to be significant in early-stage development and in lower resourced settings. For example, the Research Investment for Global Health Technology Foundation (RIGHT Foundation), a partnership between the Korean government, Gates Foundation (GF) and Korean life sciences companies, focuses on connecting companies in the Republic of Korea with LMICs. This aims to provide support for R&D of vaccines, therapeutics and diagnostics targeted at infectious diseases that disproportionately affect the developing world or that are of pandemic potential. Hilleman Laboratories, a joint venture between the philanthropic entity Wellcome Trust and industry partner MSD, focuses on developing vaccines that are affordable, accessible and highly relevant to LMICs. To further this objective, Hilleman partners the Developing Countries Vaccine Manufacturers Network (DCVMN) to facilitate technology transfer and conducts annual training in Singapore for vaccine development in LMICs.

5.3 Long-term Sustainability to Pandemic Preparedness with Smart and Agile Regulation

Most NRAs around the world face resource constraints to some extent, and this is often further strained during a public health emergency. Post COVID-19, NRAs now also face the added challenge of renewing human resources that had been depleted at least partly by the pandemic, making achieving a sustainable workforce a key priority for many NRAs moving forward[59]. This provides an impetus for NRAs to adopt smarter, agile regulation, including through regulatory cooperation.

In addition, it is unsustainable to fully decentralise and establish national vaccine production facilities in every country. This necessitates interdependent nations in a region working together for shared interests and establishing regional alliances that can serve as a valuable platform to enhance collaboration among member states.

Leveraging existing sub-regional platforms and building on them could provide an opportunity to strengthen and sustain regional pandemic preparedness efforts. Member states of ASEAN initiated the ASEAN Vaccine Security and Self-Reliance (AVSSR) in 2014. This initiative is led by the National Vaccine Institute (NVI) of Thailand, with the objective of collectively ensuring sufficient vaccines among member states, both for routine national immunisation purposes and in emergency situations. The AVSSR initiative is also an active proponent of regulatory harmonisation among ASEAN member states and regulatory systems strengthening, advocating for and recognising the integral role of regulation in sustainable vaccine manufacturing[60]. To support these efforts, the AVSSR initiative held an inaugural vaccine training workshop for ASEAN member states in September 2024, with CoRE leading the regulatory component that included regulatory capacity building and vaccine vigilance[61]. The AVSSR agenda is also included in the ASEAN Plus Three 2023-2027 cooperation work plan[62]. Implementing the ASEAN Plus Three model could offer the opportunity to tap into broader regional expertise, including the Republic of Korea's role as a global biomanufacturing leader in building regional vaccine resilience. Another sub-regional platform is the South Asian Association for Regional Cooperation (SAARC), which includes member states India and Bangladesh. Despite SAARC's prior relative inactivity, member states of the bloc came together during the COVID-19 pandemic to coordinate and share information, resources and supplies[18].

The European Commission's COVID-19 vaccine strategy can provide a potential regional model on how countries in Asia and the Pacific can work on enhancing regional cooperative mechanisms to facilitate vaccine resilience. During COVID-19, the European Union (EU) was successful in securing sufficient vaccine doses for its entire population, with coordination among member NRAs of the European Medicines Agency (EMA) supporting pan-regional vaccine rollout. While there was some criticism that vaccine rollout could have been faster, it was nonetheless a demonstration of the strength of a regional model in securing collective regional interest. The EU has since also established the Health Emergency Preparedness and Response Authority (HERA) in 2021 to coordinate pan-regional long-term pandemic prevention, preparedness and response efforts. Europe's example offers a regional model for Asia and the Pacific to consider in facilitating more effective coordination. This is in contrast to the multi-route regulatory approach that individual countries in the region had to undertake to secure sufficient COVID-19 vaccine doses for their own national populations during the recent pandemic because regional cooperative mechanisms were still under-developed[63].

With a long-term view to address issues for sustainability of the regulatory workforce, regulatory reliance is a key pillar of smart regulation[9]. For small states with lean manpower like Singapore, reliance is a pragmatic way for NRAs to augment their regulatory capacity, by relying on trusted reference NRAs to minimise regulatory burden. Reliance can be practised to varying degrees based on the level of trust built between NRAs. Work sharing, such as the joint evaluation exercises among NRAs of the ACCESS consortium (Australia, Canada, Singapore, Switzerland and United Kingdom) and ASEAN Pharmaceutical Product Working Group's (PPWG) Joint Assessment Coordinating Group, can foster trust and build deeper collaborations. This can eventually pave the way for mutual recognition agreements among equivalent NRAs, such as the agreement on GMP certificates issued by PIC/S between Singapore's HSA and Republic of Korea's MFDS[64], and among the NRAs of several ASEAN member states. These collaborations can eventually build towards strong cooperative mechanisms that are necessary for a robust and agile regional regulatory response during public health emergencies.

5.4 A Whole of Region Approach to Regulatory Cooperation

Existing regulatory platforms in Asia and the Pacific are sub-regional. There are also overlaps in the member NRAs affiliated to the various sub-regional regulatory groupings and in the scope of regulatory work covered, which can lead to duplicative efforts and potentially further widen the already diverse regional regulatory ecosystem. Hence a whole of region approach could potentially lend itself better to building the strong cooperative mechanisms that are needed to facilitate effective regulatory coordination and ensure pan-regional vaccine resilience.

The Asia-Pacific Economic Cooperation (APEC) comprises 21 major economies of the region including Indonesia, Republic of Korea and Singapore. Following the 2007 APEC Life Sciences Innovation Forum, the Regulatory Harmonization Steering Committee (RHSC) was established in 2009. The RHSC, now a subsidiary body under the APEC Sub-Committee on Standards and Conformance with the RHSC secretariat housed at CoRE, is a tripartite forum comprising government, industry and academia to encourage a favourable policy environment for life sciences innovation. The priorities of the RHSC relevant to vaccine R&D include promoting multi-regional clinical trials and Good Clinical Practice (GCP) inspection, of which CoRE is a key Centre of Excellence to facilitate training for capacity building in these areas. RHSC also draws on existing harmonisation efforts, including by the ICH and PIC/S, to

facilitate and promote regulatory convergence and cooperation, and has also identified Key Performance Indicators to help monitor the progress of convergence among member economies.

Another regulatory platform is the WHO South-East Asia Regulatory Network (SEARN), comprising NRAs of the WHO South-East Asia region that include Bangladesh, India and Indonesia. SEARN aims to promote collaboration, encourage information sharing, facilitate regulatory systems strengthening and foster convergence and reliance. Bangladesh is the current chair for the Working Group on Quality and Information Sharing, while India and Indonesia chair the Working Group on Vigilance and the Regulatory Strengthening Working Group respectively. Priority areas of SEARN's Regulatory Strengthening Work Group are promoting reliance including for vaccines and the capacity development of national regulators. As an important step to promoting reliance, SEARN members have agreed on the minimum information required from reference agencies to assess for the sameness of the pharmaceutical product being evaluated. SEARN also equips NRAs with a set of structured criteria for selection of a reference agency to expand beyond the list of legacy reference agencies, including NRAs of WHO ML 3[65].

While the sub-regional regulatory groupings of APEC RHSC, ASEAN and SEARN each contribute towards the strengthening of regulatory systems in the region, there are significant areas of overlap in scope of work covered and member states where duplicative efforts could be potentially minimised. As more countries in the region achieve functional regulatory systems and adopt internationally harmonised standards, a whole of region approach to regulatory cooperation is becoming a growing possibility for Asia and the Pacific.

The EMA and the African Medicines Agency (AMA) are examples of such regional regulatory models. However, both the EMA and AMA are specialised agencies under the mandate of the EU and African Union. In Asia and the Pacific, there is no similar supranational political and economic union to house such a regional regulatory model. Nonetheless, consistent and ongoing efforts to cooperate on building consensus through such regional models can offer potential advantages of achieving regulatory efficiencies and better addressing region-specific needs. It has been reported that such regional regulatory models could reduce regulatory approval timelines by 40-60% to facilitate timely market access, support capacity building of maturing NRAs, encourage collaborative evaluations and potentially better address region-specific needs, such as Halal certification for the ASEAN sub-region[66].

Data governance and transparency are key issues that will require consensus building in adopting a regional model for the coordinated and timely flow of information in supporting a whole of region approach to vaccine production. In this regard, a model that could serve as a helpful reference is the AVSSR initiative's plan to launch a vaccine dashboard for ASEAN member states. Three key components of the plan on data management have been outlined: data storage, analysis and processing, and data reporting. The planned dashboard is expected to facilitate the sharing of vaccine-related information among ASEAN member states, such as on various vaccine products and the stages of vaccine development in the life cycle, including on regulatory and registration information of each member state[67].

Table 4 lists the key stakeholders, associations and networks at local, regional and global level to provide a regional perspective of the entities involved in the vaccine ecosystem in Asia and the Pacific. An understanding of the entities involved can support the adoption of a coordinated and consolidated approach that could enable a wider reach and impact to be achieved for regulatory capacity building and strengthening of national regulatory systems in this region.

Table 4: Key international stakeholders and partners of the vaccine ecosystem

Philanthropic Entities and Funders	**Development Banks**
• GF • CEPI • India Alliance (DBT/Wellcome Trust) • RIGHT Foundation • USAID • Wellcome Trust	• ADB • World Bank
International and Sub-Regional Associations/Organisations	**Capacity Building Partners**
• ASEAN • ASEAN AVSSR • IVI • PATH • SAARC • WHO	• CoRE • IVI • GTH-B • NVI
Industry Networks and Partners	**Regulatory Associations and Partners**
• DCVMN • Hilleman Laboratories	• ACCESS Consortium • APEC RHSC

• International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) • WHO mRNA Technology Transfer Programme	• ASEAN PPWG • Brighton Collaboration • ICH • ICMRA • PIC/S • SEARN • United States Pharmacopeial Conventions' Promoting Quality of Medicines Programme (PQM+) • USP

6 Recommendations on Regulatory Systems Strengthening

With an understanding of the key regulatory factors, coupled with a whole of region perspective in approaching the challenges associated with strengthening of regulatory systems for sustainable vaccine manufacturing, this section provides five key recommendations to strengthen regulatory systems at a regional level.

6.1 Foster Cooperation

Challenges: Participation in regulatory platforms has been shown to build trust and foster regulatory cooperation among NRAs, particularly in the context of the regulatory systems in Asia and the Pacific. Existing regulatory platforms are often sub-regional in nature. There often exists overlap in NRAs affiliated to various sub-regional groupings and in the scope of regulatory work covered.

Recommendation: Deepening cooperation among member states within existing sub-regional multi-stakeholder alliances would be an important first step. Nonetheless, regional models are not without challenges which would need sustained efforts to boost cooperation and consensus building, including on important areas around legislative frameworks of member states and data governance. Leveraging and building on existing political and economic frameworks such as ASEAN to foster multi-stakeholder regulatory cooperation could support consensus building in addressing these issues. The regulatory efficiencies and coordination of resources from adopting a whole of region approach has the potential to better

support regulatory system strengthening in lower-resourced member states in Asia and the Pacific. While existing models in other parts of the world such as the EU and Africa are based on legislative frameworks, the principles and structures could be useful references for a multi-stakeholder regional alliance. Adapting these models to the socioeconomic and political context of Asia and the Pacific would be crucial to facilitate strengthening regulatory frameworks to enable sustainable regional vaccine manufacturing.

In addition, public-private partnerships (PPP) can be further strengthened. Collaborating with the private sector can enhance regulatory efficiency and leverage external technical expertise and insights. There are many potential areas of collaborations including providing input via public consultation of the draft regulations, collaborating in research on innovative regulatory approaches, methodologies, and standards, developing medicines for neglected diseases while ensuring affordability. PPPs are powerful approaches in the pharmaceutical regulatory field, fostering innovation, improving regulatory efficiency, and enhancing global public health. However, careful governance and transparency are essential to maximise their benefits while minimising risks.

6.2 Enhance Regulatory Agility

Challenges: While NRAs globally demonstrated regulatory agility during the COVID-19 pandemic, more can be done to build trust, share best practices and equip NRAs with the necessary tools during peacetime to facilitate an effective and agile regulatory response during public health emergencies.

Recommendation: Existing regulatory networks such as ICMRA and SEARN are important to not only provide a platform for regular exchanges among NRAs but also to build trust over time, which forms the basis for effective and agile regulatory response during emergencies. Regular exchanges during peacetime involving the sharing of regulatory best practices and innovative regulatory approaches such as a vaccine platform technology-based approach can provide NRAs with the necessary tools to be nimble in response to a public health crisis.

In addition, it is important to periodically review the need to enhance legal and regulatory framework. Augmenting legal and regulatory frameworks is essential for fostering a transparent, efficient, resilient governance system. This can be achieved by regulatory harmonisation, modernisation of regulations, closing regulatory gaps, and ensuring alignment with international best practices. Along with enhancing legal and regulatory framework,

strengthening independent regulatory bodies with adequate resources and skilled and trained professionals will support impartial enforcement which is free from political influence.

6.3 Promote Reliance

Challenges: Duplicative efforts among NRAs can contribute to regulatory burden, negatively impact the ability to respond with agility, and ultimately hinder the equitable, timely access to vaccines and other essential medical countermeasures across regional markets in a public health crisis.

Recommendation: Reliance is a pragmatic way for NRAs to augment their regulatory capacity, minimise regulatory burden and develop accelerated approval pathways while continuing to ensure quality of decision making. Regulatory networks are important platforms that support the building of trust among NRAs, encouraging increasing levels of reliance over time that can eventually pave the way for formal mutual recognition agreements. It can also facilitate broadening the list of legacy reference agencies to include other functional NRAs in the wider regional regulatory network. However, adopting reliance practice is not without challenges and does require significant investments. These include the need to invest in secure platforms such as cloud-based technologies to enable safe and timely sharing of confidential information within the regional regulatory network, guidance on data governance, and data transparency that could involve consensus building around the minimum information required in reference agencies' assessment reports to determine product sameness. More emphasis is needed to support NRAs in adopting reliance mindset and practices while at the same time adopting WHO Global Benchmarking Tool to evaluate and work towards regulatory systems strengthening towards well-functioning maturity level 3, 4 and WHO listed authority (WLA) status.

6.4 Build Regulatory Capacity

Challenges: Attaining and maintaining strong regulatory systems can be resource-intensive, particularly for NRAs that are maturing in their regulatory systems.

Recommendation: Taking reference from the WHO CIP model for capacity building, a coordinated approach among stakeholders can provide for a more resource-efficient model, although this can require some effort to coordinate resources and scope of work among stakeholders involved. A neutral, multi-stakeholder regional network could provide the practical means to facilitate coordination among stakeholders, with the opportunity to tap on the complementary scope of expertise of diverse stakeholder groups. Given the ever-evolving vaccine landscape and emerging platform technologies, industry and academic stakeholders who are at the frontier of these advancements are better poised as knowledge partners to help equip regulators with the regulatory capacity to be at the forefront of regulating latest vaccine developments.

A well-designed training programme for regulators is essential for building capacity, ensuring consistency, and improving the effectiveness of enforcement and compliance in regulatory systems. Given the diverse nature of the Asia-Pacific region, regulators must be equipped with the necessary skills, knowledge, and tools to address domestic and international challenges. For example, in the example of the reliance approach, WHO and APEC Regulatory Harmonization Steering Committee (RHSC) Centres of Excellence can lead in capacity-building initiatives. Other key areas of interest include the conduct of audits and inspections. Regulatory officials should be well-versed in the practices of conducting audits and inspections and have the necessary skills to identify violations, conduct investigations, and take enforcement action.

6.5 Facilitate Good Governance

Challenges: The diverse regulatory systems in the region can pose challenging barriers to vaccine firms seeking to access multiple regional markets in a timely manner.

Recommendation: Strong regulatory systems are a hallmark of good governance. Adoption of harmonised internationally harmonised standards provide a common understanding around vaccine safety, efficacy and quality to support cooperation and strengthening of regulatory systems. This in turn can attract investments into the region. Advanced NRAs, such as the

Republic of Korea's MFDS and Singapore's HSA, provide benchmarks and models of good governance for Asia and the Pacific, advance innovative regulatory policy, and can potentially provide leadership for coordinated regional regulatory responses during public health emergencies.

In addition, efficient enforcement mechanisms, including penalties for violations, must be backed by laws and regulations. While penalties can vary significantly from country to country, they should be sufficient to act as a deterrent against non-compliance. This may include financial fines, suspension of operations, or other administrative sanctions. Regular audits, real-time monitoring, and alternative dispute-resolution mechanisms help maintain regulatory effectiveness without overburdening legal systems.

7 The Way Forward

Despite the differences in national regulatory systems and a wide spectrum of maturity levels, Asia and the Pacific as a region has the tremendous potential and ability to strengthen its regulatory systems to support sustainable vaccine manufacturing in ensuring collective vaccine resilience. The establishment of a regional regulatory network could potentially be a way forward to securing this possible future.

To move forward with such a network, there is a need for proactive engagement of government leaders and policy makers from all relevant member states within the region, as well as with stakeholders including NRAs, industry, academia and across different government agencies beyond the health sector. Leveraging the existing political and economic frameworks of APEC, ASEAN, SEARN and others will provide support to the establishment of this network and minimise duplicative initiatives. This proposed regional regulatory network underpinned by the principles of neutrality and inclusion can provide a platform for all relevant stakeholders within the vaccine ecosystem to openly engage in contributing to building regional regulatory capacity. There are also other sociopolitical and economic benefits of this network, and further engagements are needed with relevant experts and stakeholders to map its structure and ensure sustainability.

A whole of region approach can lend itself better to coordinating efforts among stakeholders that support maturing NRAs of lower-resourced DMCs. With the ever-evolving vaccine landscape and emerging platform technologies, multi-stakeholder cooperation through a

neutral platform can more effectively facilitate the continuous regulatory capacity development needed for sustainable vaccine manufacturing. This can importantly build trust among NRAs, promote regulatory reliance and equip NRAs with the necessary tools to respond with regulatory agility during public health emergencies. As more countries in the region achieve functional regulatory systems and become more aligned to internationally harmonised standards, a whole of region approach could better address the specific needs and challenges unique to Asia and the Pacific.

In tandem with the direct support to establish such a regional regulatory network, investments in cloud-based infrastructure for data sharing will be needed to enable secure exchange of confidential information for regulatory cooperation. Interoperability of this data infrastructure, along with details around data governance, data transparency and equitable benefits of data sharing would be important considerations for deeper study.

With a common purpose of achieving vaccine and regulatory resilience, a regional regulatory network can leverage the diversity and strengths of regulatory systems in Asia and the Pacific to drive change and build a stronger regional regulatory system. The region will be stronger working together towards achieving a more equitable, just and secure future for all.

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9 Annexes

Annex I - Local Stakeholders of the Five Countries

Table 5 -7 list the health ministries, the NRAs, government agencies and government-affiliated organisations of the five countries of interest (Bangladesh, India, Indonesia, Republic of Korea and Singapore).

Health Ministries of the Five Countries

Table 5: Health ministries of the five countries

Country	Health Ministry
Bangladesh	Ministry of Health and Family Welfare
India	Ministry of Health and Family Welfare, Government of India
Indonesia	Indonesian Ministry of Health (also known as Kemenerian Kesehatan, or Kemenkes)
Republic of Korea	Ministry of Health and Welfare (MOHW)
Singapore	Ministry of Health (MOH)

National Regulatory Authorities of the Five Countries

Table 6: NRAs of the five countries

Regulatory Authority	Description
Bangladesh	
Directorate General of Drug Administration (DGDA)	- Responsible for all medical products, including vaccines - Oversees the regulation of manufacture, importation, export, domestic marketing, including the pricing of medical products
India	
Central Drugs Standard Control Organisation (CDSCO)	- Led by the Drugs Controller General of India (DCGI), an official appointed by the central government - Approval of licenses as the Central License Approving Authority - Role includes import of drugs, approval of drugs and clinical trials

Indonesia	
Indonesian Food and Drug Authority (FDA), also known as Badan Pengawas Obat dan Makanan or BPOM	- Oversees the regulation of medical products including vaccines - Also regulates supplements, cosmetics and food
Republic of Korea	
Ministry of Food and Drug Safety (MFDS)	- Oversees the regulation of medical products including vaccines - Also regulates supplements, cosmetics and food
Singapore	
Health Sciences Authority (HSA)	Comprise: - Health Products Regulation Group, of which vaccine regulation falls under this scope - Applied Sciences Group, which serves the administration of justice in forensic medicine - Blood Services Group, which secures the nation's blood supply

Government Agencies and Government-affiliated Organisations of the Five Countries

Table 7: Government agencies and affiliated organisations involved in the regulation of vaccines or vaccine policy, and their respective roles in the five countries

Government Agencies and Affiliated Organisations	Role
Bangladesh	
Bangladesh Medical Research Council (BMRC)	Established under the Ministry of Health and Family Welfare (MOHFW), it aims to promote health research in Bangladesh. Conducts ethical review and grants ethics approval of clinical trials, including Globe Biotech's domestically developed COVID-19 vaccine Bangavax. Clinical trials undergo regulatory approval in sequence from DGDA and BMRC.
Institute of Epidemiology, Disease Control and Research (IEDCR)	Also established under the MOHFW, IEDCR supports epidemiological and communicable disease testing and research services. It is Bangladesh's main centre for conducting disease surveillance and outbreak

	investigations. IEDCR has collaborations with multilateral global agencies, including with CEPI and iccdr,b to study vaccine development against the Nipah virus.
Institute of Public Health (IPH)	Formed under the MOHFW, IPH is a research and education institute that supports public health activities. The virology unit houses the National Polio and Measles Laboratory, which is designated as the national reference laboratory for environmental surveillance.
India	
Biotechnology Industry Research Assistance Council (BIRAC)	Established by the DBT as an interface agency to develop and strengthen national biotechnology research and innovations capabilities, particularly start-ups and SMEs, to address nationally relevant product development needs.
Central Drugs Laboratory (Kasauli)	One of the seven Central Drugs Laboratory under the CDSCO, the CDL Kasauli is the national centre for testing of immunobiologicals, including human vaccines. It performs lot release testing of vaccines meant for export from and import into India.
Clinical Trials Registry – India (CTRI)	CTRI is managed by the ICMR. It is a public record system for registration of clinical trials conducted in India. Clinical trial registration is mandatory in India, including multi-country trials involving India as a trial site.
Department of Biotechnology (DBT)	Established to support the building of indigenous capabilities in science and technology, including vaccine production. The regulation of biologics falls under the purview of DBT's branches, comprising RCGM, GEAC and Institutional Biosafety Committees (IBSCs), intended to ensure environmental safety.
Genetic Engineering Approval Committee (GEAC)	GEAC is a branch within DBT that is involved in the review of a biological product that contains potentially hazardous living modified organisms.

Indian Council of Medical Research (ICMR)	Coordinates biomedical research in India, including research in its thrust area of communicable diseases. ICMR has a network of research institutes, including the National Institute of Virology (NIV) for antiviral studies which is equipped with India's first Biosafety level 4 (BSL-4) laboratory.
National Board for Accreditation of Testing and Calibration Laboratories (NABL)	Provides accreditation for government, industry associations and industry, including of testing laboratories such as the CDL Kasauli.
Review Committee on Genetic Manipulation (RCGM)	Designated to review biologics that involve genetic manipulation methods.
Translational Health Science and Technology Institute (THSTI)	Affiliated with the Department of Biotechnology, THSTI is a national research institute focused on integrating medicine, science, engineering and technology into biomedical innovations. Its research centres include a Centre for Virus Research, Therapeutics and Vaccines, focusing on Dengue, Hepatitis E, HIV, Influenza, SARS-CoV-2 and Chikungunya.
Indonesia	
National Research and Innovation Agency (BRIN)	BRIN is the national research agency aimed at improving the quality of Indonesian research, technology and innovation. BRIN has several health research organisations under its purview, including the Vaccine and Drug Research Center (PRVO). BRIN cooperates with local vaccine companies such as with Etana Biotech to develop the mRNA technology locally.
Indonesian Clinical Research Centre (INA-CRC)	Central body coordinating and facilitating clinical trials across all hospitals in Indonesia.
Indonesia Clinical Research Registry (INA-CRR)	INA-CRR is under the purview of Indonesian MOH and is a registry for all clinical research conducted in Indonesia.
Indonesian National Health Research and Development Ethics Committee (KEPPKN)	Oversight of accreditation, including Good Clinical Practice (GCP) requirements of all researchers.

Republic of Korea	
Korea Institute of Drug Safety and Risk Management (KIDS)	KIDS collects, manages, analyses, evaluates and provides information relating to drug safety such as adverse drug events and drug labelling information. Adverse events are reported via the Korea Adverse Event Reporting System (KAERS), which is directed to KIDS, which then provides the information to MFDS and the WHO Uppsala Monitoring Centre (UMC).
Korea Advanced Center for Vaccine Development (KAVAD)	KAVAD is affiliated with the Korean Disease Control and Prevention Agency (KDCA), tasked to promote the domestic development of vaccines, including developing a vaccine antigen library, to prepare against emerging infectious disease threats.
Korea Disease Control and Prevention Agency (KDCA)	KDCA is formed under the MOHW with the goal of managing health risks including emerging infectious disease threats. It conducts infectious disease surveillance and promotes research and innovation including in vaccines. In 2023 KDCA announced the 'National Pandemic Preparedness and Response Plan' as a national strategy for the timely development of vaccines and other medical countermeasures in response to a pandemic.
National Institute of Food and Safety Evaluation (NIFDS)	NIFDS is formed under the MFDS to conduct regulatory science R&D, including to develop new tools, testing methods or standards used in regulating health products or in guidelines.
Korea National Enterprise for Clinical Trials Korea (KoNECT)	Affiliated with MOHW, KoNECT advances the development of clinical trial infrastructure and attracts the conduct of global clinical trials in the Republic of Korea. KoNECT's strength is its extensive, comprehensive support for global companies, including providing crucial regulatory guidance, access to clinical sites and medical professionals, providing clinical trial related training and certification.
Korea Regulatory Research Center (K-RSC)	K-RSC is affiliated with MFDS and aims to develop regulatory science professionals and the regulatory

	science field. This includes capacity building for regulatory professionals, supporting research in regulatory science and policy and strengthening partnerships between industry, government and academia both locally and globally.
Vaccine Innovative Technology Alliance Korea (VITAL-Korea)	Established in 2020 with the support of the MOHW, VITAL-Korea is aimed at promoting the discovery of novel vaccine candidates for clinical development to ensure national vaccine resilience while supporting Korea's reach to global markets. This is achieved through its three arms: 'self-sufficiency of NIP vaccines', 'vaccines of global unmet need', and 'vaccine platform technology'.
Singapore	
Agency for Science, Technology and Research (A*STAR)	A*STAR is a statutory board under the Ministry of Trade and Industry (MTI). The agency's goal is to support R&D in key areas of national need, including in human health. A*STAR Infectious Diseases Labs looks specifically into translational research including on respiratory and vector-borne diseases for infectious diseases preparedness. The Genome Institute of Singapore and Bioprocessing Technology Institute looks into product innovation, including in partnership with Hilleman Laboratories on a novel circular ribonucleic acid (circRNA) vaccine against Nipah virus.
Consortium for Clinical Research and Innovation, Singapore (CRIS)	CRIS was established in 2020 by the MOH with the goal of strengthening synergies and developing strategies for national-level clinical research and translation programmes and has six business units under it. This includes the Singapore Clinical Research Institute (SCRI) to further Singapore's clinical research landscape by coordinating clinical trials policy and processes.
Economic Development Board (EDB)	EDB is a statutory board under MTI. It is responsible for strategies that enhance Singapore's position on a global stage to sustain the country's economic growth,

	including growing the R&D sector in health. EDB was responsible for attracting major global vaccine companies into Singapore following the COVID-19 pandemic, including Thermo Fisher Scientific, Sanofi and BioNTech.
National Centre for Infectious Diseases (NCID)	NCID is a 330-bed purpose-built national facility for infectious disease management and prevention, including in outbreak management. NCID also hosts the research programme, Programme for Research in Epidemic Preparedness and Response (PREPARE) to strengthen research partnerships, including the PrepVax Office which aims to draw on these partnerships and existing vaccine development capabilities to facilitate the development of vaccine technology platforms and candidate library.
National Medical Research Council (NMRC)	NMRC provides funds for medical research to support translational and clinical research in Singapore.
Programme for Research in Epidemic Preparedness and Response (PREPARE)	PREPARE is a national programme established by the MOH to strengthen research and translational capabilities against infectious diseases threats.

Annex II - Overview of the Vaccine and Regulatory Ecosystem of the Five Countries

Overview of the Vaccine and Regulatory Ecosystem in Bangladesh

Bangladesh has a population of 175 million. Its expanded programme on immunisation (EPI) consists of 7 vaccines for 10 different pathogens, targeting 3.8 million children and 6 million women annually. Gavi provides substantial funding support for Bangladesh's EPI, which is set to be phased out from 2029 onwards. Along with the transitioning out of Gavi support, the supply disruptions during the COVID-19 pandemic and the burden of endemic and vaccine-preventable diseases have contributed to Bangladesh's drive towards vaccine self-sufficiency.

Current vaccine manufacturing capabilities are centred around Incepta Vaccine Ltd, a privately owned company which has an annual production capacity of 180 million doses. Other vaccine companies are still nascent in development, including Globe Biotech and state-owned Essential Drugs Company Limited (EDCL). To support local production of mRNA vaccines, Incepta is a recipient of the WHO mRNA Technology Transfer Programme. However, these companies are limited in accessing beyond the domestic market, which is key to ensuring long term sustainability of vaccine production. As of October 2024 at the time of this publication, Bangladesh's regulatory system has not yet attained a functional level of WHO ML 3 needed for vaccines produced locally to be considered for inclusion under the WHO prequalification programme, where these vaccines can then be purchased by global procurement agencies such as Gavi and UNICEF.

Bangladesh underwent the WHO GBT assessment in 2021 and a roadmap was laid out that addressed points raised in the IDP. To strengthen the country's regulatory systems towards achieving WHO ML 3, WHO established the Coalition of Interested Parties (CIP) to coordinate and consolidate efforts among an international network of voluntary partners to address points raised in the IDP. With international support, Bangladesh has developed vaccine lot release testing capabilities at its national control laboratory. DGDA's membership with the WHO National Control Labs Network for Biologicals facilitates the sharing of best practices, and iccdr,b is also a part of CEPI's Centralised Laboratory Network (CLN), that is aimed at standardising vaccine testing methods.

Bangladesh also receives support for vaccine manufacturing and R&D, with a partnership between CEPI, government-affiliated IEDCR and academic institute iccdr,b to study vaccine

development against the Nipah virus. However, the country will also need to continue to grow and invest in academia-industry partnerships to develop the country's vaccine R&D scene further.

Another key area of the IDP that has been largely addressed is including the necessary legal provisions which have since been incorporated into the Drugs and Cosmetics Act 2023 for the legal mandate of the DGDA on various regulatory functions including during emergency situations and to adopt regulatory reliance.

DGDA has plans to rapidly expand its regulatory workforce. To support capacity building of its national regulators, it has been receiving training from IVI on biomanufacturing including on GCP and GMP from the GTH-B program in the Republic of Korea. Training in regulatory systems strengthening should be in tandem to support the growth of the biomanufacturing workforce.

Overview of the Vaccine and Regulatory Ecosystem in India

India's vaccine regulatory system developed alongside the country's journey towards vaccine sufficiency. It is a major global vaccine producer particularly for other DMCs of the ADB, with continued strategic investments in R&D and its workforce that has built a strong bioscience ecosystem. India's large growing population have supported a strong demand for domestically produced vaccines and the country's strong vaccine regulatory system have facilitated global exports of its vaccine products.

An understanding of India's regulatory framework for R&D and clinical trials will be helpful as a consideration for other low-resourced NRAs of ADB DMCs looking to grow its vaccine R&D infrastructure as part of the end-to-end approach to sustainable vaccine manufacturing. India's national regulator CDSCO achieved WHO ML 3 vaccine-producing status in 2017. On vaccine R&D regulation, the Department of Biotechnology (DBT) was established in 1986 to build indigenous capabilities in science and technology, including vaccine production. The DBT supports the development of workforce capabilities, creation of infrastructure for R&D and the establishment of a regulatory framework for R&D. The regulation of biologics, through the branches of DBT comprising the Review Committee on Genetic Manipulation (RCGM), the Genetic Engineering Approval Committee (GEAC), and Institutional Biosafety Committees (IBSCs), was intended to ensure environmental safety. RCGM is designated to review biologics that involve genetic manipulation methods, with the pre-clinical study submitted by the research organisation's IBSC. When the biological product involves potentially hazardous living modified organisms, the GEAC is also involved.

Streamlining of regulatory approvals and the various regulatory authorities involved for R&D can be helpful to minimise regulatory burden, especially when it comes to recombinant vaccines that are unlikely to be environmentally hazardous. For example, prior to commencing pre-clinical animal studies, recombinant vaccine candidates such as mRNA or recombinant DNA vaccines like the Hepatitis B vaccine require approval from RCGM and the IBSC.

Legislation governing pre-clinical and clinical studies is contained within the New Drugs and Clinical Trial Rules, 2019. Mandatory registration of clinical trials with the Clinical Trials Registry – India (CTRI) provides transparency and accountability. For novel vaccines that are classified as Investigational New Drug (IND), the Indian Council of Medical Research (ICMR) is also involved in the clinical evaluation. Like most countries with functional regulatory

systems, India practices simultaneous review by the institutional ethics committee and CDSCO for clinical trial registration, which reduces the timeline for clinical trial approvals. India has clear clinical trial approval timelines, with priority given for drugs developed domestically and intended for local manufacture. Approval of such clinical trials is within 30 days, compared to within 90 days for drugs developed outside of India. This priority approval process is one way to encourage local R&D and manufacturing.

Overview of the Vaccine and Regulatory Ecosystem in Indonesia

Indonesia is a vast archipelagic state, with over 18,000 islands and a population of over 270 million. Thus, ensuring the health of the Indonesian population is challenging and requires coordinated national action among stakeholders. Vaccine resilience has been a key priority for Indonesia, particularly since the COVID-19 pandemic, when these efforts were accelerated. The Indonesian government proactively coordinates with national and international stakeholders involved across the entire spectrum of the vaccine lifecycle. The Indonesian MOH launched the National Vaccine Collaborating Centre (VOLARE) initiative on 26 January 2024, based on a "triple helix" researcher-industry-government collaboration. In line with this national strategy, three new private vaccine companies were established during the COVID-19 pandemic, focusing on newer vaccine platforms. These are PT Biotis Pharmaceutical Indonesia, PT Etana Biotechnologies Indonesia, and PT Jakarta Biopharmaceutical Industry (JBio). Prior to the pandemic, Indonesia's vaccine manufacturing was anchored only by state-owned company PT Bio Farma.

The augmentation of local vaccine production capabilities is intended to not only support pandemic prevention, preparedness and response but also to achieve self-sufficiency for vaccines under the NIP. At the launch of VOLARE initiative, the Ministry of Health shared that 19.7 million vials or over 100 million doses are needed per annum under Indonesia's NIP. The expanded capacity has allowed Indonesia to support over 1 billion doses per year to fulfil both domestic needs and for export. Table 8 lists the vaccine manufacturers and their respective capacities, and Table 9 lists the vaccines that are under the EPI, of which 9 of the antigens are now locally produced and 3 are in the process of development or technology transfer.

Table 8: Capacities of Indonesian vaccine manufacturers*

Manufacturer	Capacity (doses/year)	Vaccine platform
PT Bio Farma	902 million	- Inactivated - Live attenuated - Recombinant protein subunit - Polysaccharide conjugate
PT Biotis	240 million	Inactivated
PT Etana	130 million	- Nucleic acid based/mRNA - Polysaccharide conjugate - *In development: viral vector*
PT JBio	*Not yet available as JBio established in 2024*	Recombinant protein subunit

*Based on information shared at the launch of VOLARE Initiative (Jan 2024) and AVSSR Meeting (Sept 2024)

Table 9: Vaccines Listed under Indonesia's EPI

Vaccine	Age of Administration
Bacillus Calmette-Guerin, BCG*	Birth 0 - 1 month
Hepatitis B, HepB*	Birth 0 - 24 hours
Diptheria, tetanus, haemophilus influenza type B, hepatitis B, DTP-Hib-HepB*	2 months, 3 months, 4 months and 18 months
Diptheria, tetanus, DT*	6 to 7 years
Tetanus, Diptheria, Td*	7 to 8 years, 10 to 11 years (5th grade), 15 to 39 years (childbearing women)
Oral Polio, OPV*	Birth to 1 month, 2 month, 3 months and 4 months
Inactivated Polio, IPV*	4 months, 9 months
Measles and Rubella, MR†	9 months, 18 months, 6 - 7 years (1st grade)
Human Papillomavirus, HPV†	11 years (5th grade) and 12 years (6th grade) elementary school girls (Jakarta Province, Yogyakarta Province, Gorontalo, Central Java, East Java, North Sulawesi, Southeast Sulawesi, Bali, Makassar City)
Pneumococcal Vaccine, PCV*	2 months, 3 months, 12 months
Japanese Encephalitis, JE_liveAtd†	10 months (9 districts of Bali province)
Rotavirus (RV-1)	2 months, 3 months, and 4 months

*Of the vaccines listed under Indonesia's EPI, those notated with * are now locally produced, † are those that are in the process of development and technology transfer and Rotavirus vaccine being an imported product.*

During the COVID-19 pandemic, to accelerate the development of COVID-19 vaccines and augment Indonesia's resilience in pandemic response, a national team was established under Presidential Decree No. 18 of 2020 that was signed on 3 September 2020. This national team comprised senior government officials from various ministries and agencies, including the Research and Technology Ministry, National Research and Innovation Agency (BRIN), Ministry of Health, and the Indonesian FDA. Under this national team, the Merah Putih Vaccine Consortium (the national vaccine consortium taking its name from the red and white colours of the national flag) was set up.

Concurrently, the Indonesian FDA implemented accelerated regulatory pathways during the COVID-19 pandemic through the Emergency Use Authorisation (EUA) scheme, Special

Access Scheme (SAS), and providing regulatory assistance and oversight in the development, clinical trials and fulfilment of good manufacturing aspects of drugs and vaccines.

The Indonesian FDA achieved ML 3 vaccine-producing status since 2019 and was included in the transitional WLA list and thus qualified to be considered for future evaluation as a WLA[68]. The IDP developed in consultation with WHO is intended to support the Indonesian FDA in its continuing efforts in RSS and towards achieving WLA status. The ADB and CoRE has collaborated on regulatory capacity building workshops to Indonesian FDA inachieving WLA status.

Indonesian FDA becoming a WLA will help establish its role as a regional vaccine manufacturing hub, which will be very valuable for ADB DMCs. In addition, Indonesia having transited out of Gavi support in 2017 provides a reference point for other countries that are transitioning out of Gavi support such as Bangladesh to build strong regulatory capacity to support .

Overview of the Vaccine and Regulatory Ecosystem in Republic of Korea

The Republic of Korea began its journey as a global biomanufacturing powerhouse during the H1N1 pandemic of 2009. During that time, the Republic of Korea with the help of WHO was able to develop and domestically manufacture the H1N1 vaccine. Since then, there have been significant investments to develop the country's biomanufacturing sector to support local production including of vaccines and other medical countermeasures. In tandem to create a regulatory ecosystem to support the sector, Korea has also been a strong proponent of regulatory convergence and harmonisation and has supported the formation of APEC RHSC in 2009. Within a decade, the Republic of Korea has become a global biomanufacturing hub, possessing the second largest manufacturing capacity in the world.

In 2022, WHO announced the establishment of a Global Training Hub for Biomanufacturing (GTH-B) in the Republic of Korea, supporting LMICs including Bangladesh and Indonesia under the WHO mRNA technology transfer programme. These trainings, including the 'Introductory Course for Standard Practice (GxP)', were conducted by the International Vaccine Institute (IVI) also co-located in the Republic of Korea. The country's support to LMICs extends to providing funding support on R&D in biological products, including through the RIGHT Foundation, a partnership between the Korean government, GF and life sciences companies in Korea.

For its advanced regulatory system, WHO announced in 2022 that MFDS achieved ML 4 under WHO GBT assessment, the first country in the world to achieve this highest level for both vaccines and medicines regulation. In 2023, both the Republic of Korea and Singapore were among the first three countries to be recognised as WLAs, which would promote reliance processes to support maturing NRAs in the region.

Since the COVID-19 pandemic, the country has strengthened its efforts on pandemic prevention, preparedness and response while maintaining a global outlook beyond its domestic market to ensure long term sustainability. This includes boosting local vaccine R&D capabilities through the establishment of the Vaccine Innovative Technology ALliance Korea (VITAL-Korea) in 2020 that promotes national vaccine resilience for vaccines under its NIP, while also studying vaccines of global unmet need. The partnership with IVI headquartered in Seoul further strengthens the exchange of information on global vaccine research business development networks. MFDS has also introduced expedited pathways, including the Vaccine

Development-a-thon Project, and the Global Innovative products on fast track (GIFT), to expedite review of innovative products including those for public health emergencies.

With the Republic of Korea's MFDS being recognised for the highest regulatory capability and performance, there is potential for MFDS together with Singapore's HSA to provide regional leadership to advance innovative regulatory policy, model good governance and lead a coordinated regional regulatory response to facilitate timely access to vaccines and other medical countermeasures during public health emergencies.

Overview of the Vaccine and Regulatory Ecosystem in Singapore

Singapore's vaccine resilience efforts since the COVID-19 pandemic are focused on attracting investments from major pharmaceutical companies to establish vaccine research and development (R&D) and manufacturing operations in Singapore. Led by the Economic Development Board (EDB) of Singapore, this aims at meeting domestic and regional vaccine demand, particularly the surge in demand during pandemics. The new state-of-the-art vaccine facilities, such as Hilleman Laboratories' modular ACES facility primarily to support early-stage vaccine R&D in the pilot manufacturing of clinical trial materials, and Sanofi's evolutive vaccine manufacturing facility designed to rapidly and adaptably scale up production of multiple vaccine technology platforms during pandemics. With regards to laboratory capability, HSA has been an associate member of the World Health Organization (WHO) National Control Labs Network for Biologicals since September 2021. In becoming a vaccine producing country, the Health Sciences Authority (HSA) established the National Control Laboratory (NCL) Biologics Laboratory in May 2023 to support the lot release testing of locally produced vaccines.

As a boost to existing R&D capabilities on vaccines and other medical countermeasures to better deal with pandemics, the Programme for Research in Epidemic Preparedness and Response (PREPARE) was established in November 2022. PREPARE works closely with the Ministry of Health (MOH) to coordinate pandemic research with both local and international partners. Other national initiatives include the PrepVax programme which focuses on the mapping of vaccine development across both the public and private sectors, and the Biologics Pharma Innovation Programme Singapore (BioPIPS) which is a consortium which looks at R&D in biologics manufacturing to enhance manufacturing productivity and efficiency.

Singapore's national regulator HSA was the first NRA in the world to achieve WHO ML4 status. It was also one of the first three NRAs alongside with the Republic of Korea's MFDS to be recognised as a WLA. Having a lean workforce, HSA adopts a pragmatic regulatory approach and practices regulatory reliance as its key regulatory philosophy. This enables it to minimise regulatory burden and is the cornerstone of smart and agile regulation, which is critical during public health emergencies. During the COVID-19 pandemic, HSA adopted an interim authorisation approach using the Pandemic Special Access Route (PSAR), which accepted data submitted on a 'rolling' basis, to expedite the access to vaccines and other critical health products.

Singapore's HSA along with Korea's MFDS, both being recognised for the highest regulatory capability and performance, can potentially provide regional leadership to advance innovative regulatory policy, model good governance and lead a coordinated regional regulatory response during public health emergencies.

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