From Lab to Jab: Improving Asia and the Pacific’s Readiness to Produce and Deliver Vaccines

Edited by
Rupa Chanda, Pralok Gupta, and Matthias Helble
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<th>Full Form</th>
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<tr>
<td>ADB</td>
<td>Asian Development Bank</td>
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<tr>
<td>AMC</td>
<td>advance market commitment</td>
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<tr>
<td>APA</td>
<td>advance purchase agreement</td>
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<td>APVAX</td>
<td>Asia and the Pacific Vaccine Access Facility</td>
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<td>ASEAN</td>
<td>Association of Southeast Asian Nations</td>
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<td>CEPI</td>
<td>Coalition for Epidemic Preparedness Innovations</td>
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<tr>
<td>COVID-19</td>
<td>coronavirus disease</td>
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<tr>
<td>CRO</td>
<td>contract research organization</td>
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<tr>
<td>DCVMN</td>
<td>Developing Countries Vaccine Manufacturers Network</td>
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<td>ESCAP</td>
<td>United Nations Economic and Social Commission for Asia and the Pacific</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<td>FTA</td>
<td>free trade agreement</td>
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<td>HS</td>
<td>Harmonized System</td>
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<td>IP</td>
<td>intellectual property</td>
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<td>LDC</td>
<td>least-developed country</td>
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<td>MNPF</td>
<td>multinational pharmaceutical firm</td>
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<td>MOU</td>
<td>memorandum of understanding</td>
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<td>MRA</td>
<td>mutual recognition agreement</td>
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<td>NTM</td>
<td>non-tariff measure</td>
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<tr>
<td>OECD</td>
<td>Organisation for Economic Co-operation and Development</td>
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<td>PDP</td>
<td>product development partnership</td>
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<td>PPE</td>
<td>personal protective equipment</td>
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<tr>
<td>PRC</td>
<td>People’s Republic of China</td>
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<td>R&amp;D</td>
<td>research and development</td>
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<tr>
<td>SAARC</td>
<td>South Asian Association for Regional Cooperation</td>
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<tr>
<td>SDG</td>
<td>Sustainable Development Goal</td>
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<tr>
<td>SII</td>
<td>Serum Institute of India</td>
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<td>TRIPS</td>
<td>Trade-Related Aspects of Intellectual Property</td>
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<tr>
<td>UNCTAD</td>
<td>United Nations Conference on Trade and Development</td>
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<tr>
<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
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<tr>
<td>US</td>
<td>United States</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<td>WTO</td>
<td>World Trade Organization</td>
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The coronavirus disease (COVID-19) pandemic has showcased the risks and opportunities of a highly globalized world. Global interconnectedness led to a fast spread of the virus, while at the same time, the same interconnectedness enabled a fast pandemic response. Medical equipment and vaccines were quickly shipped across the world and saved millions of lives. Yet, access to those health products and technologies has not been equitable. We have witnessed large disparities in the distribution of vaccines across geographical regions and income groups of countries.

This stark inequity has triggered a rethink of health security. Governments are no longer ready to depend on the goodwill of a handful of vaccine manufacturers when fighting epidemic outbreaks. Instead, they want to ensure that they have access to vaccines and other health technologies as soon as possible. Vaccine production can then be upscaled quickly and epidemics tackled locally, in the best case to avoid pandemics. Global consensus has, therefore, emerged that the production of vaccines should be decentralized for the benefit of all.

Rebuilding the global manufacturing of vaccines is a complex undertaking. Producing vaccines is a technologically demanding process and typically relies on inputs that are sourced globally. In addition, manufacturing by itself is not enough to ensure rapid market introduction. Countries need to have the necessary regulatory capacity in place to evaluate a vaccine, as well as robust health systems that reach all people in need. This book comes at a timely moment as it attempts to provide guidance for this undertaking.

The COVID-19 pandemic will also be remembered for the breakthrough of a new technology that has been two decades in the making: mRNA. The mRNA technology has demonstrated several advantages over traditional methods of producing vaccines. However, the technology was only mastered by a few players at the outbreak of the pandemic. Asia and the Pacific was a latecomer in producing its own mRNA vaccine. Efforts to develop mRNA vaccines accelerated during the pandemic, and in several Asia-Pacific countries, these vaccines have already been approved.

In an effort to increase pandemic preparedness and response, several vaccine producers in the region are developing vaccines using mRNA or other technology platforms. This book provides a thorough overview of the different research and development (R&D) options
for vaccines. Furthermore, it addresses the important question of how best to finance the R&D of new vaccines. Another critical question is the use of flexibilities of intellectual property rights on which the book elucidates the reader.

While Asia and the Pacific is well prepared to build up its regional capacity for vaccine manufacturing, regional cooperation will be very much needed to better weather the next pandemic. Producing vaccines relies on regional and global value chains, as the book convincingly lays out. Those value chains need to keep functioning in times of crisis and, therefore, appropriate trade policies are needed. Such rules can be decided unilaterally or enshrined in regional and global trade agreements. Beyond the regional exchange of vaccines and inputs, national regulatory bodies have to work hand in hand to allow for the speedy approval of new vaccines.

The book offers highly valuable and detailed guidance on all those policy areas. I strongly believe that it will make an important contribution to enhancing future pandemic preparedness and the response of the Asia and the Pacific region. The latter is needed to minimize the huge toll on human lives, health, and the economy caused by pandemics. Considerable investments are needed to better prepare the region for the next pandemic and to ensure economic resilience and prosperity.

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1

Introduction

Rupa Chanda, Pralok Gupta, and Matthias Helble

1.1 Overview

The coronavirus disease (COVID-19) pandemic took the world by surprise. While public health experts had repeatedly warned of a disease outbreak at the global level, no country and no government was adequately prepared to tackle a health crisis of the magnitude that this pandemic created. The immediate response by governments was to provide available medical care to people infected by the disease, while at the same time deploying measures to stem the spread of the disease. Despite large scientific and technological advances over a century, many preventive measures taken in reaction to the spread of COVID-19 were similar to the 1918 influenza pandemic: physical distancing and mask wearing. In contrast to 1918, the rapid development of a vaccine targeted at SARS-CoV-2, the virus that causes COVID-19, had become a policy option; therefore, several governments resorted to the vaccine option despite technical, financial, logistical, and time constraints. Furnished with large amounts of government subsidies, academic research institutes along with pharmaceutical companies—often located in high-income countries—took the lead and started developing vaccines. Prior to the pandemic, vaccine development and its commercial release was a process that took years, sometimes spanning more than a decade. However, in the case of COVID-19 vaccines, the first vaccine was developed, approved, and released for commercial use in mid-2020, thus within less than a year from the outbreak. According to the World Health Organization (WHO), 175 COVID-19 vaccine candidates were in the clinical development phase and 199 candidates in the preclinical development phase as of December 2022 (WHO 2023).

Notwithstanding the quick development of efficacious and safe vaccines, the production of new vaccines lagged significantly behind the speed with which the virus spread. As a result, during the first 2 years of the pandemic, the world faced a significant shortage of vaccines. In the race among governments to access vaccines quickly, high-income
countries often came first, leading to a large global vaccine inequity. The United Nations Secretary-General (2022) described this unequal access to COVID-19 vaccines as the “biggest moral failure of our times”—this has led to a comprehensive rethink of pandemic preparedness and response. To achieve a more equal global distribution of vaccines, local and regional vaccine production capacity clearly needs to be strengthened to respond more effectively to future pandemic threats.

Asia, the most populous continent in the world, was one of the most affected regions in the early days of the pandemic. Although the region is a key player in global vaccine manufacturing, many Asian countries struggled to access vaccines to fight the pandemic. In addition, the technologically most advanced vaccines—mRNA vaccines—were only manufactured by two pharmaceutical companies located in the European Union and the United States. To avoid a similar situation in the future, governments in Asia and the Pacific have committed strongly to improving regional pandemic response and preparedness by strengthening local manufacturing capacity of vaccines.

To contribute to and inform these efforts, WHO, in collaboration with the United Nations Economic and Social Commission for Asia and the Pacific (ESCAP), started a research project entitled “From Lab to Jab: Improving Asia-Pacific’s Readiness to Produce and Deliver Vaccines” in the fall of 2021. This project aimed to better understand the determinants of vaccine production and delivery in Asia and the Pacific. Eight thematic papers were commissioned covering the various dimensions of vaccine production and delivery, starting from research and development (R&D), manufacturing, trade, distribution, and finally access. Apart from a thorough analysis, each thematic paper included a self-assessment guide for policy makers to identify the prevailing status, as well as bottlenecks in their countries in each of the aforementioned areas. This book is based mainly on these thematic papers and intends to provide a one-stop reference to the relevant analysis and knowledge.

We hope that the findings presented in this book will help governments in Asia and the Pacific—and other parts of the globe—to better prepare for the next pandemic as well as fight other communicable diseases. Some of the most relevant questions that this book tries to answer are the following:

- What are currently the main vaccine technologies and how do they compare with each other?
- How should vaccine R&D be incentivized and financed by the public sector?
- How is the pharmaceutical industry, which manufactures vaccines, organized, and what is the nature of existing global value chains in vaccine production?
• How do intellectual property rights promote or hinder the development of vaccines?
• What kind of logistics infrastructure is needed to ensure the safe and seamless transport of vaccines across borders?
• How does trade policy affect the manufacturing and availability of vaccines?
• How can access to vaccines be improved between and within countries?

This book is intended as a useful resource for governments and policy makers, academic and research institutions, think tanks, international organizations, industry, as well as the general public. Though the policy inputs and recommendations in various chapters of this book are primarily based on the current pandemic, they can be a useful resource to prepare for future pandemics. For instance, compressing the vaccine development cycle from a few years to a few months has significant implications for how governments and industry conduct vaccine R&D. Similarly, the implications of intellectual property rights and trade barriers for vaccine availability are important for policy makers to consider and address.

1.2 Background and Motivation

Prior to the COVID-19 pandemic, vaccine production received limited attention. Vaccines were considered medical products that are given mostly during childhood for prevention of diseases. Vaccines for adults were rarely thought of as an instrument for averting a health crisis. However, the COVID-19 pandemic shifted the focus to vaccines, being targeted initially for the adult population and later for children, as vaccines were the only means of tackling the health shock the world faced in 2020 and 2021. Therefore, health professionals, researchers, economists, trade professionals, and lawyers started analyzing the different aspects involved in vaccine production and their availability.

Vaccine production is a complex and time-consuming exercise involving, among others, R&D, clinical trials, global sourcing of essential inputs, intellectual property issues, specialized skills, and transport, including dedicated vehicles and equipment for proper handling and storage. While vaccines were an important tool in this pandemic, access to lifesaving vaccines was a key challenge many countries had to face. Barring a few countries, which had the technical and financial capacity to produce vaccines domestically, most countries were dependent on imports. Thus, trade emerged during the pandemic as an important means to distribute the vaccines from the few producing
countries to the billions of people across the globe, although the vaccines were still subject to a number of regulatory approvals as well as tariff and non-tariff barriers.

Given the complexities involved in the production and distribution of vaccines, it is important to analyze the complete vaccine production cycle, especially in the context of COVID-19 vaccines. Such an analysis can help governments to prepare better for future pandemics. With these objectives in mind, this book presents an analysis of the various aspects of vaccine production and distribution from end to end: from R&D, financing, and intellectual property and global value chains, which affect the development and production of vaccines, to transportation and logistics, international trade, investment and trade agreements, and regulatory cooperation, all of which affect the availability of these vaccines across borders, and finally to the role of national health systems, which impact equitable access to vaccines and their distribution within countries.

This book focuses on Asia and the Pacific, though it also provides an overview of the global landscape as regards vaccine availability and access. Most chapters use the ESCAP definition of Asia and the Pacific, which includes 58 regional member states and associate members. The member states covered by the analysis vary by chapter, reflecting data availability as well as relevance for the specific research questions. The choice of Asia and the Pacific is motivated by the fact that it includes two of the world’s major developing country producers of vaccines—India and the People’s Republic of China—and the region is also an important source of raw materials for global vaccine production. From a public health perspective, Asia and the Pacific is home to 60% of the world’s population\(^1\) and therefore a significant demand center of vaccines. However, most of the countries in this region do not have the capacity or technical know-how to produce vaccines. Therefore, most countries in the region depend on the import of vaccines to fulfill their domestic needs. Thus, on various counts, the region presents a good case study to analyze the various issues associated with equitable and affordable access to vaccines and can provide useful insights for practitioners and researchers in this domain.

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\(^1\) According to data from the United Nations Population Fund.
1.3 Overview of Chapters

This book combines the knowledge produced through the ESCAP–WHO joint project on vaccines with work by authors outside the project to address the topic comprehensively. After this introductory chapter, the book has 10 chapters, which deal with selected aspects of vaccine production and delivery and a concluding chapter highlighting policy recommendations.

Chapter 2 by Antonio Postigo focuses on vaccine R&D. The COVID-19 pandemic has highlighted both the strengths and weaknesses of national, regional, and global vaccine R&D systems. The author shows that translating public and private R&D efforts into effective vaccines in a timely manner requires not only sufficient financial and scientific resources but also a policy-driven R&D ecosystem that fosters innovation, public–private partnerships, and international cooperation. Furthermore, traditional platforms to produce vaccines are significantly slower than newer vaccine technologies (mRNA, DNA, and viral vectors) as they involve a biological process rather than a chemical one that mRNA or DNA vaccine platforms use. Although R&D for mRNA vaccines requires an advanced technological setting and expertise, once the technology is set up, mRNA vaccines have lower marginal R&D and manufacturing costs and can be more easily redesigned for new variants of a pathogen. The economics behind vaccine R&D has common features with those for therapeutic drugs. On the supply side, vaccine production is capital intensive and creates a barrier to new entrants, impeding competition. On the demand side, and unlike therapeutic drugs, preventive vaccines are administered only once or a few times during one’s lifetime. The above factor reduces the profitability of many vaccines, disincentivizes multinational pharmaceutical firms from investing in vaccine R&D, and ultimately results in a market failure where the overall supply of vaccines falls below the socially optimal amount. However, unlike most therapeutic drugs, vaccines generate positive externalities for the population at large. Cost–benefit analyses of investment in vaccine R&D must take into account the social benefits of vaccines. The chapter analyzes some strategies to stimulate investments in vaccine R&D at several levels, including the prioritization of targets in the vaccine R&D pipeline, as well as supply- and demand-side approaches to overcome market failures in vaccine R&D.

Chapter 3, also by Antonio Postigo, discusses policies to promote vaccine R&D in the specific context of Asia and the Pacific. The region accounts for the largest share of global R&D spending, but vaccine R&D and the vaccine pharmaceutical industry vary greatly from country to
country. While the United Nations Educational, Scientific and Cultural Organization (UNESCO) East and Southeast Asia region represents 40.4% of global R&D expenditures, 44 countries in the ESCAP region are recipients of official development assistance for medical research and the health sector. Governments of many high- and middle-income countries in the region offer grants to universities and research institutes to carry out early stages of biomedical R&D and to boost university–industry ties. In several countries, state-owned vaccine manufacturers control a significant part of the domestic vaccine market and conduct R&D and production of high-quality vaccines. At the same time, many countries in the region, including low- and middle-income countries, have a vibrant domestically owned private pharmaceutical industry that is involved not only in the manufacturing of vaccines but in many cases also in conducting vaccine R&D. The COVID-19 pandemic showed the possibilities for international cooperation but also its potential fragility. International cooperation in R&D during the pandemic was in part possible because of previously existing informal networks and formal institutional linkages between different stakeholders. Several regional and subregional institutions and intergovernmental organizations in Asia and the Pacific also helped promote and coordinate regional cooperation in vaccine R&D. The chapter proposes several policy actions to foster partnerships between relevant stakeholders at the national, regional, and/or subregional levels. Governments can promote academia–industry ties through several interrelated policies and regulations to strengthen R&D funding programs for joint projects between universities and the private sector, and regional and subregional intergovernmental organizations can play a more active role in coordinating the policies and actions of their members in vaccine R&D. The chapter also develops policy recommendations to increase pandemic preparedness and response of national and regional vaccine R&D systems, including using regional approaches for the pooling of funding for R&D.

Chapter 4 by Gavin Yamey, Kaci Kennedy McDade, Wenhui Mao, and Chukwunomso Ekene Osakwe focuses on financing R&D for new vaccines in developing countries in Asia and Pacific. The authors first highlight that for many infectious diseases, such as HIV and hookworm infection, that have a high burden in the region, there are no licensed and effective vaccines. In addition, for some neglected infectious diseases in the region, such as dengue and malaria, the existing vaccines have limitations. For example, although over 2 billion people are at high risk of malaria in Asia and the Pacific and the disease is endemic in 17 nations in the region, the only licensed malaria vaccine has low efficacy against clinical malaria. One reason behind the lack of vaccines
is the financing gap, especially for late-stage trials. The authors estimate an annual financing gap of around $2 billion for vaccine R&D in the case of neglected infectious diseases and about $50 million–$170 million in the case of emerging infectious diseases. The authors then examine the current financing landscape for vaccine R&D in Asia and the Pacific, focusing on strengths and weaknesses, the main funding sources and recipients, recent initiatives aimed at raising financing (e.g., public–private partnerships), and the levels of funding that have been mobilized. They examine the value proposition for increased investments in vaccine R&D in Asia and the Pacific. Finally, they propose policy options to close the financing gap for vaccine R&D in the region, covering resource mobilization mechanisms, pooling approaches, and strategic purchasing.

**Chapter 5** by Andrew Mitchell, Antony Taubman, and Theodore Samlidis discusses the implementation of flexibilities in the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) to spur vaccine production. For most COVID-19 and other vaccine technologies, manufacturing capacity remains highly concentrated in a handful of countries. Many studies attribute the inequitable and delayed distribution of vaccines at least partly to unevenly distributed production. Along with other factors, such as sustainable financing, regulatory clearance, and logistical capacity, expanding and diversifying vaccine production entails leveraging access to technology platforms such as novel mRNA technologies, viral vectors, and recombinant protein vaccines. In turn, working with such technologies entails access to various inventions, know-how, and regulatory data as part of a broader technology transfer process. Much of this subject matter is protected by intellectual property rights across multiple jurisdictions. This chapter shows how to potentially overcome real or purported intellectual property barriers to regional vaccine production. In particular, it examines how governments can utilize intellectual property flexibilities for increasing and diversifying the manufacture and distribution of COVID-19 vaccines. Concrete examples illustrate how these flexibilities are practiced in a range of domestic jurisdictions in Asia and the Pacific, together with practical recommendations on various policy aspects.

**Chapter 6** by Pralok Gupta and Ayona Bhattacharjee analyzes trade barriers to vaccines and vaccine inputs in the context of Asia and the Pacific and provides insights from an analysis of the trade in vaccines and related inputs. The COVID-19 pandemic took the world by surprise, resulting in huge demand and supply shocks for different goods and services, particularly for vaccines and their related inputs. Since many countries were not able to produce vaccines or did not have sufficient
supply of vaccine inputs, international trade became an important means
to improve the availability, accessibility, and affordability of vaccines
and related inputs across countries. The chapter analyzes various
dimensions of trade and trade-related barriers affecting vaccines and
vaccine inputs in Asia and the Pacific, which is second only to Europe
and Central Asia in terms of the major regional traders of vaccines
and related inputs. Using the joint indicative list of critical inputs for
COVID-19 vaccines, published by the WTO in 2021, the authors analyze
the trade trends and patterns during 2000–2020 for vaccines and
three broad groups of vaccine inputs: vaccine manufacturing, vaccine
administration, and vaccine storage and distribution. They identify the
leading exporters and importers, the most traded vaccine inputs, and
inter- or intraregional trade in vaccines and related inputs. Further,
regulatory restrictions to protect public health also affected vaccine
trade flows, despite high demand during the pandemic. The chapter
analyzes tariff and non-tariff measures, highlighting the persistence of
several regulatory measures that were imposed prior to the COVID-19
pandemic. The secondary data analysis is combined with insights from a
primary survey of stakeholders concerned with vaccine production and
trade in India, which as a significant player for vaccines in Asia and the
Pacific, offers useful insights and takeaways for other trading countries.
The authors conclude the chapter by highlighting the need for several
measures, such as diversifying import sources of vaccines and vaccine
inputs, tariff reduction, elimination of export restrictions, regulatory
coherence, and increased transparency concerning non-tariff measures
to jointly improve immunization across countries.

**Chapter 7** by Pavida Pananond and Alvaro Cuervo-Cazurra discusses
global value chains in vaccine production and local production capacity.
The COVID-19 pandemic highlighted the crucial role of vaccines
in public health management, economic development, and national
security. Reflecting on the experience producing and distributing
COVID-19 vaccines provides lessons for future preparedness and
vaccine capacity building. The authors deliberate two main approaches
to vaccine production: internalization-driven production, whereby the
leading multinational pharmaceutical firms control most of the vaccine
production in a few locations; and externalization-driven production,
whereby lead companies spread their vaccine production across various
regions. Selection criteria are driven by a combination of factors, including
vaccine technology, strategy and missions of the vaccine producers, and
availability and capacity of qualified contract manufacturers in host
countries. Readiness for vaccine production depends on an interaction
of factors at the firm, value chain, and country levels. Countries can
prepare for the next pandemic through various means, of which local
production is just one. Countries with sufficient technological capacity can focus on participating in production. The more complex the stage of vaccine production, the higher the need for technological capacity. Countries with limited technological capacity need instead to focus on ensuring speedy access to vaccines, regardless of where they are produced. Meanwhile, countries with higher technological capacity should collaborate with developed and developing economies to ensure speedy global production and distribution. The ultimate objective of a vaccine policy is speedy and efficient administration of vaccines to the population, though domestic production should not be considered as a preferred means for ensuring the efficient and fair distribution of vaccines.

Chapter 8 by Rawinkhan Srinon, Duangpun Kritchanchai, and Thananya Wasusri discusses the challenges of international transport and logistics of vaccines and vaccine inputs for Asia and the Pacific. These challenges include barriers in the form of export process limitations and restrictions on inputs and raw material imports, cumbersome regulatory approval processes, and delays due to customs and security control requirements. Additionally, the authors show that ensuring efficient shipment routes can also be problematic, especially when countries are in lockdown. Another major challenge is the lack of cold chain capacity for traditional, frozen, and ultra-cold vaccines, particularly in low-income and lower middle-income countries in the region. Complying with different requirements and procedures for temperature management and control of different vaccines during transport and cross-border processing are key for a successful vaccine supply chain, but a major obstacle for most countries. Consequently, countries need to maintain cold chain integrity along the supply chain and implement transparency and visibility through track and trace systems. The chapter focuses on six recommended action areas to ease cross-border processes for both vaccines and vaccine inputs: facilitation and security of cross-border processes; cold chain facility and equipment readiness; cold chain workforce capability; cooperation and coordination among governments and key stakeholders; working with logistics experts; and appropriate information technology systems such as track and trace systems to ensure information sharing and monitoring of cold chain integrity.

Chapter 9 by Arpita Mukherjee and Eshana Mukherjee discusses trade, investment, and cooperation in the health sector, with focus on vaccines in Asia and the Pacific. The authors note that the region continues to be one of the fastest-growing in the world, even though the COVID-19 pandemic has caused a global economic slowdown. Accompanied by supply chain and trade disruptions, the pandemic
highlighted the need for greater trade, investment, and cooperation in the region to aid recovery. Consequently, countries have signed several trade agreements since 2020. As the pandemic progressed and the COVID-19 vaccine was developed and approved, the global demand for medical goods shifted. While ventilators, testing kits, and personal protective equipment were shipped at the beginning of the pandemic, trade in products critical for administering vaccines, such as rubber gloves, syringes, and needles, increased sharply later on, rising from 10% in the first quarter of 2020 to over 18% in the second quarter of 2021. Countries that successfully exported health products to fight the pandemic also witnessed an increase in foreign direct investment inflows, while the rest of the region saw a decline of over 20% in 2020.

The chapter discusses the importance of trade investment and cooperation in the health sector and vaccines to address the pandemic and prepare for future health shocks. Regional trade agreements signed in Asia and the Pacific have limited coverage of health-related goods and services, although the region accounts for 48% of all regional trade agreements in the world. COVID-19 vaccine production and administration are hampered by features of such agreements, such as long phaseout periods for tariffs, high autonomous tariffs, rigid rules of origin, lack of mutually recognized standards and professional degrees, lengthy approval procedures, lack of transparency in government procurement, and compliance issues related to the WTO TRIPS Agreement. To help build a resilient supply chain and make COVID-19 vaccines easily accessible to all, the chapter presents several policy recommendations for member countries to leverage existing trade and other arrangements to facilitate trade and investment flows in the health-care sector and engage in mutually beneficial collaboration.

Chapter 10 by Simon Lacey and Andrew Mitchell highlights the need for regulatory cooperation in vaccines among countries in Asia and the Pacific. The COVID-19 pandemic ushered in significant progress in terms of innovation and cooperation between national regulatory authorities, which came under immense pressure to rapidly approve vaccines in order to both bring the pandemic under control and mitigate the crippling socioeconomic impact the pandemic unleashed on every country. Previously, regulatory cooperation between national regulatory authorities had been an ongoing and incrementally evolving concern, but the COVID-19 crisis forced regulators to make a virtue out of necessity, increasing their recourse to networking, work sharing, and relying on both WHO and other national regulatory authorities. Collaboration in Asia and the Pacific also allowed for sharing of knowledge and resources and led to the adoption of new approaches and workflows. The authors ask whether the innovations adopted during the recent pandemic will lead to fundamental and lasting
changes in both mindset and operational procedures—or whether national regulatory authorities will simply revert to the pre-pandemic modus operandi. The former outcome, though arguably the most desirable, may be too much to hope for given bureaucratic inertia and the lack of continued political pressure and will to reform approval procedures now that the pandemic has been largely vanquished.

Chapter 11 by Valerie Gilbert Ulep discusses the importance of national health systems strengthening to improve the distribution of and access to vaccines, with a focus on addressing inequities in access to COVID-19 vaccines in Asia and the Pacific. Countries in the region have been severely affected by the pandemic. The economic and health recovery of countries in the region hinges on the rapid and equitable deployment of safe and effective COVID-19 vaccines. As of the time of writing, 60% of the population in the region has been fully vaccinated, with a large variation across and within countries. Vaccination coverage in high-income countries in the region was 80% compared to 10% in low-income countries. While some countries were administering booster shots, the poorer countries in the region were yet to achieve their coverage targets for the primary series. The author highlights the relevant literature on health systems and argues that vaccine inequity is a serious threat to public health and the global economy. Allowing the populations of certain countries to remain unprotected increases the risk of continuous viral transmission and mutation, leading to a patchy economic recovery. Previous public health emergencies and epidemics (e.g., influenza outbreaks in 2004 and 2009) had brought to light the problem of accessing lifesaving vaccines and drugs in developing countries. With the COVID-19 pandemic, a concerted effort was made to address the problem by creating the COVID-19 Vaccine Global Access (COVAX) facility. However, COVAX was not enough to prevent global vaccine inequity, as competition between countries for the procurement of vaccines led to cases of vaccine nationalism. In addition, to avoid vaccine inequity within countries, governments need to improve the readiness of the national health systems to confront the next pandemic.

1.4 Conclusion

The COVID-19 pandemic has taught us many lessons pertaining to health care. One of these relates to the development, availability, distribution, and administration of vaccines. Though cases have significantly gone down in 2022 across most countries, the pandemic is not yet over. In December 2022, the People’s Republic of China, the Republic of Korea, Brazil, and the US, among other countries, have started reporting a sudden increase in COVID-19 cases. Therefore, COVID-19 vaccines and
their lessons are still important and significant in our fight against the pandemic.

Asia and the Pacific has significant potential to build resilience and response capacity to confront a new pandemic threat. The region has the technical know-how, raw materials, and financial resources, which when combined with the commitment by many governments in the region to improve pandemic preparedness, hold the promise that vaccine inequities can be substantially reduced. In addition to the region’s two existing major vaccine producers, India and the People’s Republic of China, other countries are likely to increase their capacity for vaccine production in the near future. This trend will thus help to reduce the asymmetry in the availability of vaccines within and outside this region through enhanced production and supply of vaccines and vaccine inputs through trade. Furthermore, our analysis in this book shows that the vaccine recipient countries need to eliminate or reduce tariff and non-tariff barriers to trade in vaccines and related inputs. Regulatory cooperation among governments through intergovernmental efforts or with the support of international organizations, such as ESCAP and the Asian Development Bank, can further spur trade in vaccines and related inputs. Against this backdrop, this book is an attempt to bring together relevant information on the many facets of vaccine access, distribution, and affordability to provide useful insights to governments, policy makers, and practitioners and enable better preparedness and response to future pandemics.
References


PART I

Research and Development of Vaccines
The Economics and Actors in Vaccine Research and Development

Antonio Postigo

2.1 Introduction

Despite great progress over the recent decades, millions of people in developing countries die each year from infectious diseases—in particular communicable diseases—most commonly caused by viruses, bacteria, and parasites, because of the lack of effective vaccines and/or treatments.\(^1\) Infectious diseases not only cause disability and cost lives, but also affect livelihoods, hamper social and economic development, and affect global security. In 2019, several countries in Asia and the Pacific were among those with the highest “burden of disease” from infectious diseases (GBD-CN 2020; GBDI-2019C 2020).\(^2\) Although there are no figures on the overall “cost of illness” from infectious diseases in Asia and the Pacific (Shah et al. 2020), eliminating malaria alone would save more than 400,000 lives and generate economic benefits totaling almost $90 billion (Shretta et al. 2019).\(^3\) In this context, vaccine

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1. As detailed later, most vaccines are used to prevent infectious diseases (prophylactic or preventive vaccines), but some are used to treat diseases (therapeutic vaccines) like cancer and chronic diseases. This report focuses primarily on the research and development (R&D) of preventive vaccines for infectious diseases and, therefore, refers to biological or synthetic products designed to generate an immune response in the recipient to prevent an infection.

2. The “burden of disease” quantifies the impact of living with illness and injury and dying prematurely. It is often expressed as disability-adjusted life years, which indicate the years of healthy life lost from death and illness.

3. The “cost of illness” measures the medical and other costs that result from a specific disease or condition.
development has become a key component of any multipronged strategy to control the spread of infectious diseases and combat their impacts. Once available, vaccines are also among the most cost-effective public health interventions. They have contributed to reducing mortality and morbidity from infectious diseases and generated significant cost savings for health systems.

The composition and participants encompassed in the research and development (R&D) ecosystem vary among authors (Keusch and Lurie 2020). Keusch and Lurie (2020) describe R&D as a “series of non-linear mini-ecosystems, each with particular characteristics, business needs, and incentives, pathways, problems, barriers, and proponents, each influencing one another.” In its broadest sense, R&D comprises the set of activities, actors, and institutions that begins with upstream research (fundamental discovery research in fields like microbiology and immunology), continues with preclinical research, and concludes with clinical research. Some scholars also include in the R&D ecosystem the regulatory approval and manufacturing stages; still others expand R&D to global access to newly developed drugs, vaccines, and diagnostic kits, as well as the global financing mechanisms to ensure access for those who cannot afford them.

2.2 R&D in Vaccines: Vaccine Technologies, Stages, and Main Actors

2.2.1 Main Types of Vaccines and Technology Platforms

Most vaccines contain two components: the antigen (all or part of the infectious pathogen) or a precursor of the antigen (the genetic component of the pathogen: DNA or RNA), and the adjuvant (a product that stimulates the immune system in the person receiving the vaccine to generate a stronger response) (reviewed in Ahmed, Ellis, and Rappuoli 2018; Iwasaki and Omer 2020). In addition, the vaccine solution contains preservatives and stabilizers to extend the shelf life of the product. Vaccine R&D is mainly focused on identifying the most appropriate antigen (or its precursors) and adjuvants to include in the vaccine preparation (Ahmed, Ellis, and Rappuoli 2018).

Recent advances in genome sequencing and bioinformatics approaches have reduced the time and costs of vaccine design and development. In addition, gene synthesis and automation technologies now allow a part or the whole genetic code of pathogens to be synthesized rapidly and relatively inexpensively. For instance, in the context of the COVID-19 pandemic, these technologies have been used to synthesize in the laboratory the most antigenic parts of the genome of SARS-CoV-2
(those that were predicted to generate the strongest immune response)—and of any variants arising over time—and use the synthetic material as a source of viral particles instead of having to rely on clinical samples.

There are different types of vaccines with different implications for the complexity of their R&D and manufacturing (Iwasaki and Omer 2020; Pollard and Bijker 2021) (Table 2.1). Vaccines containing live attenuated and/or inactivated or killed versions of the pathogen or an inactive version of a toxoid produced by the pathogen were first introduced more than a century ago. Vaccines that contain a subunit of

<table>
<thead>
<tr>
<th>Type of Vaccines</th>
<th>First Time Used</th>
<th>Advantages</th>
<th>Challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live-attenuated pathogen</td>
<td>1798</td>
<td>Long-lasting protection</td>
<td>Safety and stability issues</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Most do not require an adjuvant</td>
<td></td>
</tr>
<tr>
<td>Killed pathogen</td>
<td>1896</td>
<td>Most do not require an adjuvant</td>
<td></td>
</tr>
<tr>
<td>Toxoid</td>
<td>1923</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subunit (protein, peptide, polysaccharide)</td>
<td>1970</td>
<td>Can be tested quickly</td>
<td>Require an adjuvant</td>
</tr>
<tr>
<td>Virus-like protein</td>
<td>1986</td>
<td></td>
<td>Require an adjuvant</td>
</tr>
<tr>
<td>Viral vector</td>
<td>2019</td>
<td>Strong protection</td>
<td>Preexisting immunity against vector</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do not require an adjuvant</td>
<td>Potential challenges still not completely known</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Replicable manufacturing</td>
<td></td>
</tr>
<tr>
<td>Nucleic acid (DNA, RNA)</td>
<td>2020</td>
<td>Strong protection</td>
<td>Potential challenges still not completely known</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do not require an adjuvant</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Replicable manufacturing</td>
<td>Unstable and easily degraded</td>
</tr>
<tr>
<td>Antigen-presenting cells (dendritic cells), T cells</td>
<td>2020</td>
<td>Approved by the United States Food and Drug Administration for therapeutic used in cancer</td>
<td>Potential challenges still not completely known</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterial vector</td>
<td></td>
<td>Lasting protection</td>
<td>Not yet approved for use in humans</td>
</tr>
</tbody>
</table>

Sources: Ahmed, Ellis, and Rappuoli (2018); Iwasaki and Omer (2020); and Pollard and Bijker (2021).
the pathogen (e.g., a protein or a fragment of a protein, either purified or synthetically produced) or a virus-like particle (viral proteins that resemble a native virus but lack the viral genome that allows virus replication) became available in the 1970s and 1980s. Gene synthesis and automation technologies have made it possible to develop and manufacture viral vectors and nucleic acid-based (RNA, DNA) vaccines much faster than traditional vaccines. The COVID-19 pandemic has spurred the introduction of mRNA vaccines for the first time for use in humans (Iwasaki and Omer 2020; WHO 2021) (Table 2.1). Instead of introducing the pathogen or fractions of it, mRNA and DNA vaccines induce the recipient to produce the viral proteins on their own. Except for some live-attenuated vaccines that generate live-lasting protection, most vaccines require additional booster shots.

The production of classical vaccines (e.g., live attenuated, killed, subunits) is not only slower than for nucleic acid-based vaccines but also involves a biological process rather than a chemical one, which entails greater variability in yield and performance from one batch to another. The manufacturing of classical vaccines is also more prone to batch contamination compared to the production not only of therapeutic drugs but also of viral vector-based and nucleic acid-based vaccines (Douglas and Samant 2018). The greater biological variability in the yield and performance of vaccines compared to therapeutic drugs also means slower approval by regulatory authorities and, as detailed later, precludes a market for generic vaccines such as the existing one for therapeutic drugs. As discussed in the following sections, these technical challenges create uncertainty for potential vaccine developers and manufacturers and are important economic disincentives that can lead to fewer (or no) firms interested in vaccine R&D and manufacturing, and to manufacturing failures and supply shortages.

In contrast, mRNA vaccines can be designed more rapidly once the genetic code of the pathogen is available and can be more easily updated and redesigned to take into account new variants of the pathogen. Although the manufacturing of mRNA vaccines requires advanced gene synthesis technologies and expertise—which are still lacking in many countries—their production is largely a chemical process that does not depend on the growth of the pathogen or the culture or cells, so their production is easier to scale up and can be performed more consistently (Jackson et al. 2020). These features of mRNA vaccines explain why they were the first to be developed and approved for COVID-19 (WHO 2021). They also have other advantages relative to traditional platforms. First,
mRNA vaccines are safer because their production does not require the inactivation of the infectious pathogen. Second, in mRNA vaccines, a fragment of the pathogen is produced by our cells, thus promoting a more effective immune response and without the need of adding an adjuvant. Third, mRNA vaccines are easier to redesign to account for new variants of the pathogens. And fourth, once the technology is set up, the high consistency in the production process and the trend toward lower costs as the technology progresses mean low marginal costs of R&D and manufacturing (Pardi et al. 2018; Knezevic et al. 2021). The World Health Organization (WHO) has played a key role in setting standards regarding the quality, safety, and efficacy of traditional vaccines; different initiatives are currently being considered to reach a similar consensus in the manufacture and regulation of mRNA vaccines (Knezevic et al. 2021). One of the drawbacks of mRNA vaccines relative to traditional vaccines is that they are more labile and require cooler storage conditions, which are not always available in remote and/or low-income settings. In any case, mRNA vaccines are opening a new era in vaccinology whose implications in the fight against infectious diseases, as well as other diseases and conditions (e.g., anti-cancer vaccines), are still unforeseen.

Vaccine developers across Asia and the Pacific have successfully developed candidates and commercial vaccines for COVID-19 using most of the existing technologies, including new platforms such as viral vector vaccines, and several companies in the region are now working toward developing and manufacturing mRNA-based vaccines (see Chapter 3).

### 2.2.2 Stages of Vaccine R&D

Although the vaccines for Ebola virus disease were developed in around 5 years and several of the vaccines for COVID-19 in less than a year, for most vaccines, it can take up to 10–15 years to obtain a safe and efficient candidate. Vaccine development comprises several stages (Figure 2.1), most overlapping with the stages involved in developing therapeutic drugs (Leroux-Roels et al. 2011; Douglas and Samant 2018; Artaud et al. 2019).

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5 Being a newer platform, mRNA vaccines also raise new issues regarding intellectual property rights protection that are addressed in Chapter 5 of the book. WHO, the Medicines Patent Pool initiative, and several African international partners have established an mRNA Vaccine Technology Transfer Center for the production of mRNA vaccines for Africa, and WHO plans to establish similar centers in other regions (Medicines Patent Pool 2021).
From Lab to Jab: Improving Asia and the Pacific’s Readiness to Produce and Deliver Vaccines

The first step in vaccine R&D is the discovery stage (2–4 years), which involves basic research in a laboratory to define an appropriate vaccine technology and identify what elements (antigen targets) in the infectious agent can best trigger an immune response in the individual receiving the vaccine. Recent technological advances (compound library screening, bioinformatics, spectrometry, crystallography, artificial intelligence, etc.) can predict which regions in the pathogen interact with human antibodies for structure-based vaccine design. The second is the preclinical stage (1–2 years) when laboratory animals are subjected to an early version of the vaccine to assess in vivo both its safety and immunogenicity potential. The third is the clinical trials stage, during which vaccine candidates are administered to humans to test that they are safe and provide effective protection in different human populations (different cohorts by age, sex, ethnic group, etc.). Clinical trials are lengthy (8–10 years), costly, and subject to strict regulatory and ethical standards that are set by the corresponding regulatory authorities and vary from country to country. In turn, clinical trials comprise several phases: Phase I (around 2 years), in which vaccine candidates are tested for safety and immunogenicity in 10–50 healthy volunteers; Phase II (2–3 years), during which 200–500 individuals participate in randomized trials where some individuals receive a placebo while others receive vaccine candidates to monitor their effective dosage, safety, and immunogenicity; Phase III (5–10 years) involves thousands of people in randomized placebo and vaccine cohorts and in which a selected vaccine candidate is approved for use. Phase IV (more than 10 years) involves post-market surveillance and safety monitoring.

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6 Also called immunogenicity: production of antibodies and/or a cellular response against the antigen.
candidate is assessed for triggering an immune response and preventing infection in the context of an outbreak. Unlike with drugs, vaccines that pass phases II and III have a high probability of achieving licensure. Phase III requires rigorous analysis and management and constitutes the mainstay over which regulatory authorities approve or deny the use of the vaccine in a specified target population. In most cases, vaccine manufacturers scale up production only after licensure. Even after the vaccine is on the market, manufacturers must continuously conduct pharmacovigilance of the vaccine (Phase IV) to evaluate its safety, the degree of long-term protection it provides, and investigate potential new indications (different schedules, the need for boosts, etc.). Likewise, the competent authority will continue to monitor vaccine production facilities and review testing processes.

In contrast to therapeutic drugs, which are designed to treat a person who is already ill, most vaccines aim at preventing a particular disease and are administered to large populations of healthy people. Consequently, the threshold to accept adverse secondary effects in preventive vaccines must meet more stringent safety requirements to gain regulatory approval, requiring longer and more expensive clinical trials. In this chapter, the term “vaccine” is used to refer to preventive vaccines.

Basic preclinical-clinical R&D of vaccines must be closely integrated with manufacturing R&D, which includes process and assay development. Process development involves the manufacture of vaccine samples that comply with regulatory requirements for use in humans, preclinical toxicology testing, analytical assessment, and technological transfer for consistent manufacturing and scale-up from a pilot plant to final locations for large-scale batches (Douglas and Samant 2018). Assay development refers to the definition of benchmarks regarding the purity of vaccine components, stability, consistency of production batches, and tests to predict vaccine efficacy. Since Phase III clinical trials are expensive, lengthy, and require large numbers of people, certain analytical correlates of vaccine immunogenicity and disease protection (e.g., blood levels of antibodies) have been proposed as possible alternatives or complements to Phase III trials of some vaccines (Plotkin 2010). Nevertheless, the adoption of these correlates requires approval by the corresponding regulatory authorities.

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7 In this particular aspect, therapeutic vaccines to fight cancer, allergies, and certain chronic diseases are similar to therapeutic drugs.
2.2.3 Main Actors in Vaccine R&D

In recent years, vaccine and drug R&D has witnessed the emergence of new actors and new forms of interactions between them. The actors involved through the different stages of vaccine R&D are relatively similar to those in R&D for therapeutic drugs:

(i) **Discovery research.** This is typically carried out in basic research laboratories at universities, research institutes, and, increasingly, in small start-up biotechnology companies.

(ii) **Preclinical research.** Automation in sequencing and small-molecule synthesis has allowed basic research laboratories and biotech firms to become increasingly involved not only in vaccine design but also in the production of small samples of pathogen subunits or adjuvants to test in preclinical animal models. Alternatively, once a proof of concept has been designed, vaccine samples for preclinical trials are produced by pharmaceutical firms or in collaborations with basic research laboratories.

(iii) **Clinical trials and pharmacovigilance.** Pharmaceutical firms are responsible for carrying out phases I–IV of clinical trials through agreements with clinics and hospitals, or, increasingly, outsourcing to contract research organizations (CROs).

In many countries, particularly high- and upper middle-income economies, **government agencies** are the major source of direct funding for discovery and preclinical research for drug and vaccine development (Viergever and Hendriks 2016), which increasingly implies partnerships with private firms. In the case of vaccines for diseases that affect primarily the developing world, governments in developed economies fund health R&D directly, through official development assistance, or via partnerships with philanthropic foundations and international organizations. For instance, product development partnerships (PDPs)—nonprofit organizations that coordinate public and private stakeholders—are now one of the main players in vaccine and drug R&D for endemic, neglected, and emerging infectious diseases.

Within the **private sector**, the landscape of actors involved in vaccine R&D is changing because of the mergers and consolidations among the largest multinational pharmaceutical firms (MNPFs), the proliferation of biotech companies and CROs, and the increased participation of pharmaceutical firms in developing countries. During the 15 years before the COVID-19 pandemic, the number of new vaccines developed by MNPFs remained stagnant, while those developed by small biotech
firms doubled and those developed by emerging-market pharmaceutical firms experienced a 13-fold increase (Aars, Clark, and Schwalbe 2021). MNPFs are often feeding their pipelines through licensing and/or acquisitions of smaller biotech firms.

Most multinational pharmaceutical firms that conduct R&D for vaccines also do so for therapeutic drugs. The largest MNPFs have within the firm all the required expertise in clinical R&D, data and project management, and regulatory affairs (Douglas and Samant 2018). Since some of these tasks are now carried out by CROs, MNPFs are focusing their expertise and financial efforts on vaccine design, process and assay development, registration, and manufacturing.

Many small biotech companies involved in vaccine R&D began as start-ups that academic scientists established with funding from venture capitalists often matched by government programs, with the vast majority based in developed countries. As most of these small biotech firms have limited expertise in process and clinical development and manufacturing, they often partner with and/or license their vaccines and/or technology platforms to MNPFs (Douglas and Samant 2018). Some of the recent advances in vaccinology have been introduced by small biotech firms. For example, technological innovations in vaccines for hepatitis B and *Haemophilus influenzae* type b were developed by small biotech companies that later became associated or acquired by larger MNPFs (Douglas and Samant 2018). In 2018, BioNTech AG, a biotech company specializing in mRNA technologies, partnered with Pfizer to jointly conduct R&D for mRNA-based influenza vaccines, with Pfizer taking sole responsibility for clinical development and commercialization. More recently, during the COVID-19 pandemic, BioNTech, along with Moderna emerged as key players in mRNA vaccines.

A total of 41 public and private pharmaceutical firms in developing countries are part of the Developing Countries Vaccine Manufacturers Network (DCVMN). In 2019, companies in the network had an estimated capacity of 3.5 billion doses for more than 50 vaccines, 13 of them prequalified by WHO and eligible for procurement by United Nations agencies (Hayman and Pagliusi 2020; Hayman, Suri, and Prasad 2021; DCVMN website). Although most of these firms have relatively limited financial and expertise capabilities, some have been able to develop second-generation vaccines without formal technology transfer (Aars, Clark, and Schwalbe 2021). Many DCVMN firms conduct vaccine R&D through partnerships, including PDPs (as discussed later), with philanthropic foundations and larger pharmaceutical companies. During the pandemic, several DCVMN members have developed
COVID-19 vaccines on their own and/or manufacture them through partnerships with MNPFs—for instance, the Serum Institute of India teamed up with AstraZeneca for the manufacturing of COVID-19 vaccines in India. Nevertheless, a recent survey among DCVMN firms regarding their R&D capabilities indicated that most require funding and/or technical transfer for the newest mRNA vaccines (Hayman, Suri, and Prasad 2021).

The first contract research organizations emerged in the 1940s, but their number, size, and roles have expanded enormously since the 1990s (Dimachkie-Masri et al. 2011; Balconi and Lorenzi 2017; Gad, Spainhour, and Serota 2020). Initially, MNPFs only outsourced to CROs their clinical research activities to enhance the cost benefits and to expand the geographical reach of clinical trials. Most of the major CROs are now taking on new tasks, from participating in preclinical vaccine research stages to preparing applications for ethical committees, institutional review boards, and regulatory authorities. In 2018, the global CRO market stood at $38.4 billion, but this number has likely increased significantly since then, as many of the COVID-19 vaccines were developed with support from CROs. The involvement of CROs in health R&D goes often unnoticed, because contract relationships between pharmaceutical firms and CROs are confidential since the former, particularly the largest MNPFs, rarely acknowledge the participation of CROs in their clinical trials.

In the context of health emergencies, global and regional intergovernmental organizations can coordinate the policies and actions of governments, strengthen disease surveillance, and share information and best strategies. But intergovernmental organizations also have important functions in vaccine R&D. In May 2015, in the aftermath of the 2014 Ebola virus disease epidemic, WHO convened a group of experts to develop the R&D Blueprint for Action to Prevent Epidemics (WHO 2016, 2017). The initiative aims to strengthen R&D preparedness (before a health threat) and R&D response (during an outbreak) with the ultimate goal of reducing the time between a disease outbreak and the approval of efficient vaccines, drugs, and diagnostic tools. To that effect, the WHO R&D Blueprint prioritizes diseases with the greatest epidemic potential and/or for which no or insufficient diagnostic, preventive, and curative solutions exist and develops an R&D road map for each of these diseases (WHO 2016, 2017; Mehand, Al-Shorbaji, et al. 2018; Mehand, Millett, et al. 2018; WHO 2021). Diseases with ongoing R&D programs or product pipelines are not included in the priority list. Among the prioritized diseases is the so-called Disease X, which refers to a serious international epidemic caused by a pathogen currently unknown to cause human disease. The
The Economics and Actors in Vaccine Research and Development

R&D Blueprint aims at developing crosscutting R&D preparedness that also covers Disease X.

The emergence and proliferation of **product development partnerships** has transformed the R&D landscape for diseases affecting the developing world. PDPs are nonprofit, legally independent partnership organizations that were introduced in the late 1990s as a form of private–public partnership to address failures in the vaccine and drug markets and the lack of economic incentives for pharmaceutical firms to undertake R&D for neglected diseases affecting developing countries (as discussed in section 2.3) (Widdus 2001; Hayter and Nisar 2018; Taylor and Smith 2020; Bulc and Ramchandani 2021). PDPs channel funding from high-income countries and philanthropic foundations and engage academic research laboratories and pharmaceutical firms in conducting vaccine and drug R&D to develop at affordable costs vaccines, drugs, and diagnostic tools for diseases in developing countries. For instance, one of the first PDPs was established to develop a meningococcal conjugate vaccine by the Serum Institute of India with funding from the Bill & Melinda Gates Foundation and technical assistance from PATH. PDPs use management practices in their R&D activities and coordinate partners through R&D stages, allocate financial resources to the most promising vaccine development projects, and manage the project portfolio. Most PDPs have in-house R&D capabilities, conduct capacity building and technological transfer, and carry out advocacy, and some have manufacturing capacities. To minimize risks in vaccine R&D, they use a portfolio approach and simultaneously develop multiple vaccine candidates for a single disease. PDPs focus on one or several diseases, though some do not aim at any particular disease. Rather, they promote R&D that can accelerate vaccine and drug R&D on several diseases—for instance, new mouse models for preclinical research, diagnostic tools, benchmarks for clinical trials, and harmonized biological standards and assays (Aars, Clark, and Schwalbe 2021). In 2018, R&D funding for emerging infectious diseases reached $886 million, with 65.2% for vaccine development and 95.7% directly from the funders to vaccine and drug developers (Policy Cures Research 2021a). In contrast, 23% of the $3.9 billion global investments in R&D for neglected diseases were channeled through PDP and non-PDP intermediaries (Policy Cures Research 2021b).

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8 There are three main types of health-related private–public partnerships (PPPs): (i) access PPPs that aim to expand access to existing products but for which there is limited demand or ability to pay; (ii) systems-based PPPs, whose goal is to improve the capacity of health systems; and (iii) PDPs (Taylor and Smith 2020).
PDPs can be distinguished from other non-PDP intermediaries—often referred to as “virtual companies” or “social capital venture funds”—that also direct funding for R&D in poverty-related diseases to vaccine and drug developers. In contrast to PDPs, they rely on external partners for R&D. The largest of these non-PDP intermediaries is the Coalition for Epidemic Preparedness Innovations (CEPI) that channels funding for vaccine R&D for priority diseases identified in the WHO R&D Blueprint.

The Global Research Collaboration for Infectious Disease Preparedness (GLoPID-R) is a global alliance of 32 funding organizations (government agencies, philanthropic foundations, and non-PDP intermediaries) that finance R&D to develop vaccines, drugs, and diagnostic tools for new or reemerging infectious diseases. Its goal is to facilitate an effective R&D response within 48 hours of a significant outbreak. GLoPID-R itself does not fund R&D; instead, it promotes the sharing of information and addresses scientific, logistical, legal, regulatory, ethical, and financial challenges that underpin an international R&D response. WHO, CEPI, the European & Developing Countries Clinical Trials Partnership, and ESSENCE on Health Research⁹ are observers in the global alliance.

2.3 The Economics of Vaccine R&D

Vaccine production is a highly capital-intensive industry, which represents a barrier to new entrants and competition. A WHO study calculated that the cost for setting up a plant to produce monovalent vaccines in a high-income country stands at between $50 million and $500 million and rises to $700 million for polyvalent vaccines (Lobo 2021). Projecting the costs and profits in vaccine R&D and manufacturing is also more difficult than in other industry sectors (Aars, Clark, and Schwalbe 2021). The cost of progressing a vaccine through the end of Phase II of clinical trials has been estimated at $112 million to $469 million (Gouglas et al. 2018). R&D costs for newer technology vaccines are higher at all stages, as developers must recover discovery and/or preclinical research investments, as well as obtain regulatory approvals and plant certifications. In contrast, for traditional technologies, older vaccines, and modifications of existing vaccines (e.g., influenza variants), many fixed costs have been recouped (Lobo 2021).

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⁹ ESSENCE on Health Research is an initiative of TDR, the Special Programme for Research and Training in Tropical Diseases, cosponsored by the United Nations Children’s Fund (UNICEF), the United Nations Development Programme, the World Bank, and WHO.
Liability risks are also higher for newer vaccines and technologies. The biological nature of most vaccines with the corresponding variability in yields, the larger size of clinical trials, and the stricter regulatory requirements make vaccine R&D more lengthy and costly than R&D for therapeutic drugs. On average, the time to develop a traditional vaccine, from the preclinical stage to its entry into the market, is 10.7 years and the market entry probability of a vaccine candidate is 6% (Pronker et al. 2013).

As noted, the R&D, manufacturing, and sales of new vaccines are highly concentrated in a few large MNPFs located in high-income countries, the so-called vaccine production hub (Evenett et al. 2021). In 2013, around 70% of global vaccine sales were in the United States (US) and the European Union (Douglas and Samant 2018). Historically, MNPFs have shown more interest in developing new therapeutic drugs than in new vaccines. In 2019, global vaccine sales totaled $35.2 billion, just 3.5% of the entire pharmaceutical market (Evaluate 2020; Lobo 2021). Nevertheless, vaccine sales are growing faster, having tripled since 2005—compared to an 80% growth of drug sales—owing to the introduction of new vaccines with high volumes and margins (e.g., hepatitis B, multivalent diphtheria–tetanus–pertussis [DTP], pneumococcal, human papillomavirus [HPV], and zoster) and many low-income countries gaining access to vaccines funded through official development assistance, philanthropic foundations, and international organizations (Evaluate 2020; Douglas and Samant 2018). The COVID-19 pandemic has increased these figures; some market studies estimated that in 2021 the COVID-19 vaccine market alone in the US, Japan, and the five largest European economies amounted to $13.1 billion and that in 2024 may reach $25 billion for the entire world (GlobalData 2021; Market Study Report 2021).

The economics behind vaccine R&D and manufacturing are influenced by supply and demand factors (Sloan 2012; Lobo 2021). On the supply side, pharmaceutical firms must consider the opportunity cost of investing their financial, human capital, and manufacturing assets in the R&D of a particular vaccine compared to doing so in therapeutic drugs (or other vaccines) with higher prospects of success and/or returns on investment. As noted earlier, compared to therapeutic drugs, developing a new vaccine involves stricter safety requirements, which increase the costs and time of clinical trials. Additionally, since most vaccine and drug candidates eventually fail, pharmaceutical firms usually wait to collect data on safety and efficacy before scaling up manufacturing (which requires specific sunk investments), also delaying the eventual availability of vaccines and drugs. For instance, most COVID-19 vaccine candidates will never reach the market.
While the availability of multiple vaccines and platforms ensures that several of them will be safe and effective, simultaneous investment in too many candidates can have diminishing returns.

On the demand side, some factors are common between vaccines and therapeutic drugs, and some are different. The demand for vaccines and therapeutic drugs is affected by disease prevalence and pathogen infectiveness, as well as people’s willingness and ability to pay, which are reduced in socioeconomically vulnerable populations in developing countries. However, unlike therapeutic drugs, particularly those for treating chronic conditions, preventive vaccines are administered only once or a few times during a lifetime. Evidence also indicates that individuals—and often government health programs—are more willing to pay for treatment than for prevention (Kremer and Snyder 2015). The lack of predictable demand for a vaccine, particularly in resource-scarce developing countries, creates uncertainty about returns on investment, precluding or delaying the development of vaccines. While some vaccines (e.g., pediatric vaccines, influenza, COVID-19) are in high demand, vaccines for many neglected infectious diseases affecting developing countries have relatively low demand, a factor that is compounded by the lower ability to pay by those that need them. Similar economic factors apply when it comes to outbreaks of emerging infectious diseases, which tend to start in low-income countries and are also plagued by unpredictability and uncertainty regarding their nature, geographical location, and potential spread and duration—thus, the incentives of firms to invest in R&D preparedness (Nuzzo et al. 2019).

Although most analyses conclude that the economic incentives to develop new vaccines are low, the incentives should be assessed on a case-by-case basis and there are also arguments pointing to high profit margins for vaccines (Douglas and Samant 2018; Lobo 2021). First, many vaccines are produced by a limited number of manufacturers—36 vaccines have two or fewer suppliers prequalified by WHO—thus generating higher margins. Second, in contrast to therapeutic drugs, yield and batch variability in biological vaccines force new entrants to conduct new clinical trials and obtain regulatory approvals, so the vaccine market is not amenable to the production of generics. Consequently, the holders of vaccine intellectual property rights enjoy monopoly rents for a longer period than for therapeutic drugs. Third,

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10 This concentration is the result of the business structure of the vaccine market with high fixed costs, price-sensitive demand, and dynamic quality competition (Danzon and Sousa Pereira 2011). New pharmaceutical firms in Brazil, India, and the People’s Republic of China have increased the sources of vaccines for developing countries, particularly for traditional vaccines (WHO 2021).
vaccines that have been on the market for a long time have low marginal costs per dose and high cost-effectiveness ratios. Empirical evidence indicates that stronger protection of intellectual property rights does not necessarily promote public–private partnerships for vaccine R&D if stakeholders are not prepared to cooperate (da Veiga et al. 2016). Likewise, linking tax reductions to R&D investments may be more attractive for pharmaceutical and biotech firms than grants.

Unlike most therapeutic drugs, vaccine R&D and manufacturing generate benefits (positive externalities) for the population at large, even globally, because most vaccines prevent contagion and also protect unvaccinated individuals (Gersovitz and Hammer 2003; Endarti and Riewpaiboon 2016; Younes et al. 2020). As with any externality, individuals that have not received the vaccine do not pay for this additional benefit and pharmaceutical firms have no way to charge for this societal benefit, thus creating a gap between private (pharmaceutical firms) and social (society) rates of return (Younes et al. 2020; Endarti and Riewpaiboon 2016).

Some of the abovementioned factors reduce the profitability of many vaccines (particularly those for diseases afflicting populations in low-income countries), the incentive for MNPFs to invest in such vaccine R&D, and ultimately the overall supply of vaccines (below the socially optimal amount), thus creating a market failure. Cost–benefit analyses of investment in vaccine R&D must take into account (internalize in economic terms) the positive social benefits of vaccines (Vu et al. 2020). Like downstream investments in free immunization programs, upstream investments in vaccine R&D must consider the impacts of immunization beyond its health benefits. When the broader societal impacts of immunization (e.g., long-term disability burden, economic productivity, education) are considered, the estimated net return to vaccination programs ranges from $16 to $44 for every dollar spent in free vaccination programs (Bärnighausen et al. 2014; Ozawa et al. 2016).

### 2.4 Strengthening Incentives for Vaccine R&D

#### 2.4.1 Prioritization of Targets in the Vaccine R&D Pipeline

To build and strengthen R&D preparedness, national governments, as well as regional and subregional intergovernmental organizations, should first identify which infectious diseases to prioritize for vaccine R&D. The vaccines included in most national immunization programs have been around for a long time, can be procured from multiple
sources, and can be produced at relatively low marginal costs. Countries with vaccine manufacturing capacity should aim to conduct R&D and produce these vaccines domestically or coordinate their production at the regional and/or subregional level. Similar recommendations apply to other vaccines with large target populations even if they are not included in national immunization programs (e.g., influenza vaccines).

Prioritization is particularly important in emerging infectious diseases with high epidemic potential. As no single country, including high-income economies, can invest in R&D for all potential emerging pathogens, regional cooperation is particularly important for these infectious diseases. Disease prioritization is not always straightforward and requires establishing clear criteria. The WHO R&D Blueprint has developed a comprehensive methodology of R&D prioritization to ensure that its list of selected diseases best reflects targeted global health needs and focuses on the most pressing threats based on their epidemic potential and for which there are no, or insufficient, countermeasures. This methodology used by WHO is readily available and draws on established best practices and national and regional experience. It is similar also to the methodology that CEPI uses to prioritize its vaccine R&D targets (WHO 2016; Mehand, Al-Shorbaji, et al. 2018; Mehand, Millett, et al. 2018; Gouglas and Marsh 2019; Jonkmans, D’Acremont, and Flahault 2021; Kojom and Singh 2021). In developing countries lacking the expertise to implement this methodology, WHO, through its regional offices, donor countries, PDPs and non-PDP intermediaries, and/or international organizations (e.g., United Nations Economic and Social Commission for Asia and the Pacific [UN-ESCAP], scientific associations), can provide technical assistance and capacity building of policymakers responsible for health and science, technology, and innovation.

For existing diseases of predominantly domestic or subregional and regional prevalence, which disease to prioritize should be guided by several parameters: (i) prevalence and burden and cost of illness of each disease (e.g., case fatality, disability-adjusted life years, economic impacts) in the country, the region (e.g., Asia and the Pacific), or subregions; (ii) its infectiveness and potential for epidemic and pandemic spread; (iii) the global status of R&D for each disease; (iv) the existence, availability, and cost of other vaccines; (v) other qualitative, intangible, or subjective criteria depending on the stakeholders; and, importantly, (vi) the financial viability and R&D capacity to generate new vaccines (Andre 2002; WHO Regional Office for South-East Asia 2003; Mehand, Millett, et al. 2018; Gouglas and Marsh 2019; Jonkmans, D’Acremont, and Flahault 2021; Sharma 2021).

The prioritization of R&D investments should also include building preparedness for still-unknown pathogens (Disease X). Most of
the newly emerging human infectious diseases are caused by viruses that jump from other animals (zoonotic diseases). Of the estimated 1.6 million viruses affecting animals, only a small number can infect humans. Identifying in advance and including in prioritization lists pathogens in animals with a high risk of infecting humans is key to develop R&D preparedness for the next zoonotic threat. Advances in genomic sequencing, bioinformatics, and artificial intelligence are being used to assess the risk of human infection by viruses that have not yet jumped to humans (Mollentze, Babayan, and Streicker 2021).

2.4.2 Overcoming Market Failures in Vaccine R&D

The possibility of a market failure supports external interventions and/or regulation of the vaccine market. Prospective vaccine buyers (usually, governments, PDPs and non-PDP intermediaries, or international organizations) can bear part of the risk and incentivize firms to invest in R&D and/or scale up vaccine production before R&D and regulatory approval are completed by subsidizing the cost of R&D and/or new production facilities and stimulating the supply of vaccines (supply side or push strategies). Alternatively, potential buyers can stimulate vaccine demand by introducing regulations that increase vaccine uptake and/or by committing to purchase doses after regulatory approval (demand side or pull strategies). As with other global common goods, individual countries have an incentive to free ride on the vaccine R&D investments of other countries. Although this additional market failure also occurred in the context of the COVID-19 pandemic, many governments—including middle-income countries—have funded R&D programs for COVID-19 vaccines, and their willingness to pay has been high as countries compete to gain early access to vaccines (Younes et al. 2020).

Multiple supply-side approaches are used to address potential failures in the vaccine market. The most common strategy is funding vaccine R&D through public and/or philanthropic sources. Governments can incentivize vaccine R&D by increasing funding for basic and preclinical research in universities and public research institutes. While there may be a case for government intervention and regulation to address market failures in R&D and manufacturing of vaccines for some diseases, establishing the optimal level of public funding and support for R&D is not straightforward (Younes et al. 2020). Targeted funding for vaccine R&D can potentially result in diminishing returns and overinvestment, as well as the diversion of resources to other diseases. Most low-income countries lack the financial resources to invest in vaccine R&D and/or the physical infrastructure and/or human capital required for R&D investments to be productive and effective. As noted earlier, for countries
with limited economic resources to address other social and economic challenges, it is neither possible nor sensible to invest in the early stages of vaccine R&D or to develop an advanced vaccine pharmaceutical industry. PDPs and other non-PDP intermediaries have proliferated as an innovative mechanism to fund vaccine R&D. In situations where it is deemed important to involve developing countries in later stages of vaccine R&D (e.g., clinical trials) and/or because of other factors (e.g., size of the country, geography, epidemiological status), WHO, regional intergovernmental organizations, regional scientific societies, and PDPs can provide technical training and/or financial resources to these countries to develop and strengthen vaccine R&D though improvements in the physical infrastructure and human capital.

Other supply-side mechanisms to encourage pharmaceutical firms to invest in vaccine R&D include regulatory, policy, tax, and direct financial incentives. For instance, milestone subsidies—for when companies successfully complete an R&D stage—have been applied successfully. Governments can also explore other supply mechanisms short of grants like tax incentives for investing in vaccine R&D. Strengthening intellectual property right protection can also incentivize firms to invest in vaccine R&D and manufacturing, though this can result in higher prices and generate equity problems with lower access for low-income countries (see Chapter 5). Policy reforms to ensure a fast-track review of vaccine candidates by regulatory authorities in the context of health emergencies also ease uncertainty for firms to invest in vaccine R&D by accelerating the time and reducing the cost of clinical trials, particularly of Phase III trials that involve large numbers of people. For instance, in several vaccines, efforts have been made to validate analytical parameters as proxy measurements of immune protection, thus reducing the number of people required in clinical trials (Plotkin 2010; Aars, Clark, and Schwalbe 2021). However, any potential relaxation of the regulatory framework of clinical trials should ensure the safety and effectiveness of approved vaccines. Other supply-side strategies include public–private partnerships in R&D at the national or international level (see Chapter 3), and technology transfer from multinational corporations to indigenous start-ups and small and/or medium-sized private firms.

Demand-side approaches that increase the final demand for vaccines also incentivize firms to invest in R&D. One way to address market failures and de-risk and incentivize vaccine R&D investment by pharmaceutical firms—and, in some cases, directly fund R&D—is through the use of a financial commitment—advanced market commitments (AMCs) and advanced purchase agreements (APAs)—to subsidize the future purchase of a vaccine that is not yet available,
at an agreed-upon price and contingent upon the development of an efficient and safe vaccine. APAs are contracts between a pharmaceutical manufacturer and buyers (governments, international organizations, philanthropic foundations, PDPs, and non-PDP intermediaries) whereby buyers commit to purchasing a product once the product is developed, approved, and brought to the market, thus guaranteeing that there will be a market for the product even before the product is available (Turner 2016; Boulet et al. 2021). Buyers benefit both from speeding up vaccine R&D and securing doses at a predictable price. APAs do not only de-risk R&D investment, but they can also fund capacity building for scaling up manufacturing and directly finance R&D. AMCs can also be supply-side approaches when they directly finance R&D and/or the scale-up of manufacturing. The terms of reference of APAs vary widely by contract and are usually confidential. Increased production capacity remains a permanent benefit for the firm, and late-stage (e.g., clinical trials) R&D costs, when the APA covers these, do not have to be refunded if a product is not successful or approved by the regulatory authorities (Boulet et al. 2021). At the same time, APAs do not require the intellectual property generated by the firms to be shared, licensed, or co-owned with the buyer. In return, APAs impose conditions on pharmaceutical firms regarding the number of doses and time line of the delivery. AMCs were first used in 2009 when Gavi, the Vaccine Alliance; UNICEF; and the World Bank pledged $1.5 billion to incentivize the development and supply of pneumococcal vaccines in low-income countries. Since then, APAs/AMCs have been used to accelerate the development and supply pandemic influenza and Ebola vaccines (Turner 2016). APAs are part of global pandemic influenza preparedness, and some countries pay an annual “pandemic preparedness fee,” which cost is not publicly available, to the manufacturer to maintain the contract (Turner 2016). APAs have become even more popular during the COVID-19 pandemic with many high-income and upper middle-income countries signing APAs with vaccine developers to procure COVID-19 vaccines (Pharmaceutical Technology 2021). PDPs and non-PDP intermediaries have also used AMCs successfully to incentivize R&D for neglected and emerging diseases.

Overall, APAs have proven successful in de-risking investments by pharmaceutical firms in R&D and building manufacturing capacity, thus accelerating the ultimate development of vaccines. Ahuja et al. (2021) found that early at-risk investments yield large benefits for countries across all levels of income, including low-income countries that would be otherwise priced out of the market. Buyers should diversify vaccine candidates and platforms and provide both supply-side approaches like payments for only part of the total cost—to ensure that firms have
a stake in the risk and success of vaccine development—and demand-side approaches structured in ways to incentivize speed. On the other hand, pharmaceutical firms may be discouraged from investing in R&D when governments and PDP and non-PDP intermediaries, as the main purchasers of vaccines, use their bargaining power and often the government’s regulatory prerogative to bring prices down to levels close to the marginal cost of manufacturing and distribution which does not cover vaccine R&D (Sloan 2012). In addition, as firms have to fulfill their delivery commitments to buyers—most often developed countries—before producing doses for countries without APAs, such agreements can impact equity in access to vaccines in developing countries. This highlights the need for international organizations and initiatives (e.g., CEPI, COVAX, Gavi) to engage in APAs/AMCs to serve low-income countries.

Other demand-side strategies include increasing vaccine uptake through information campaigns, free vaccination programs, and/or mandatory vaccinations. In most countries, vaccines included in recommended or mandatory national immunization programs, as well as those required during epidemics and pandemics, are administered free of charge by the government. The impact of mandatory vaccinations on vaccine uptake is still open to debate, and countries need to consider whether compulsory programs can be effectively implemented and enforced or whether recommendations and incentives work better.

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11 The prices paid by high-income countries tend to be above the prices offered in tenders organized by UNICEF and other organizations purchasing vaccines for distribution in low-income countries.
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3

Vaccine Research and Development in Asia and the Pacific: Strengthening Partnerships among Actors at the Domestic and Regional Levels

Antonio Postigo

3.1 Introduction

Economic growth in most countries in Asia and the Pacific in the past 2 decades has contributed to slowing the spread of most infectious diseases, including neglected and newly emerging infectious diseases. At the same time, increasing urbanization, food insecurity, and/or political instability have worked in the opposite direction. While many neglected tropical diseases (e.g., malaria, typhoid fever, schistosomiasis, leishmaniasis, rabies) have been declining in Asia and the Pacific in recent decades, others (e.g., dengue, echinococcosis) have increased (Hotez 2020).

The Sixty-Fifth World Health Assembly in May 2012 endorsed the Global Vaccine Action Plan 2011–2020, which declared the 2010s the Decade of Vaccines with the goal of a world in which all individuals and communities enjoy lives free from preventable diseases through vaccines (WHO 2013). The importance of research and development (R&D) in biomedical and health-care innovation has always been widely recognized and further heightened by COVID-19, the disease caused by SARS-CoV-2. Developing strong vaccine R&D capacity is essential to achieving Goal 3 of the Sustainable Development Goals (SDGs) (“Ensure healthy lives and promote well-being for all at all ages”) and other SDGs related to healthy people and populations. Specifically concerning SDG targets 3.3 and 9.5, the United Nations General Assembly adopted
resolution 71/313, which includes several indicators that highlight the importance of ending communicable diseases and enhancing R&D through investment and capacity building (Table 3.1).

### Table 3.1: Vaccines and the Sustainable Development Goals

<table>
<thead>
<tr>
<th>Sustainable Development Goals</th>
<th>Targets</th>
<th>Indicators</th>
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<tbody>
<tr>
<td><strong>Goal 3</strong>: Ensure healthy lives and promote well-being for all at all ages</td>
<td>3.3: By 2030, end the epidemics of AIDS, tuberculosis, malaria, and neglected tropical diseases and combat hepatitis, water-borne diseases, and other communicable diseases</td>
<td>3.3.1 Number of new HIV infections per 1,000 uninfected population, by sex, age, and key populations</td>
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<td></td>
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<td>3.3.2 Tuberculosis incidence per 1,000 population</td>
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<td>3.3.3 Malaria incidence per 1,000 population</td>
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<td>3.3.4 Hepatitis B incidence per 100,000 population</td>
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<td></td>
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<td>3.3.5 Number of people requiring interventions against neglected tropical diseases</td>
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<tr>
<td><strong>Goal 9</strong>: Build resilient infrastructure, promote inclusive and sustainable industrialization, and foster innovation</td>
<td>9.5: Enhance scientific research, upgrade the technological capabilities of industrial sectors in all countries, in particular developing countries, including, by 2030, encouraging innovation and substantially increasing the number of research and development workers per 1 million people and public and private research and development spending</td>
<td>9.5.1 Research and development expenditure as a proportion of gross domestic product</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9.5.2 Researchers (in full-time equivalent) per million inhabitants</td>
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</tbody>
</table>

3.2 Main Indicators in the Biomedical and Vaccine R&D in Asia and the Pacific

3.2.1 R&D Input Indicators: Expenditures and Human Resources in Vaccine and Biomedical Research

In this chapter, Asia and the Pacific refers to the region comprising 49 of the 53 full members of the United Nations Economic and Social Commission for Asia and the Pacific (ESCAP). France, the Netherlands, the United Kingdom, and the United States, although full members of ESCAP, are not considered part of the “Asia and the Pacific economies” group in most of the figures and tables within this chapter. Economic diversity within the ESCAP region is also reflected in its health indicators as well as in R&D investment for biomedical research. More than 80% of ESCAP members are recipients of official development assistance for medical research and basic health sectors (SDG indicator 3.b.2) (Figure 3.1). Of all World Health Organization (WHO) regions, the Western Pacific has the highest per capita average for indicator 3.b.2. At the same time, Asia and the Pacific accounts for the largest share of global R&D spending. The United Nations Educational, Scientific and Cultural Organization (UNESCO) East and Southeast Asia region alone—led by the People’s Republic of China (PRC), Japan, and the Republic of Korea—represents 40.4% of global R&D expenditures, followed by North America (27.4%) and the European Union (18.7%) (Figure 3.2) (UNESCO 2021; UIS website). Four ESCAP members are among the world’s top 15 economies with the highest R&D spending as a proportion of gross domestic product (GDP) (SDG indicator 9.5.1): the Republic of Korea (4.5%), Taipei, China (3.3%), Japan (3.2%), and the PRC (2.1%). For instance, they are ahead of the corresponding figure in the United Kingdom and the average in Europe Table 3.2 (UIS website; WHO Global Observatory on Health R&D; UNESCO 2021). Health R&D as a share of GDP in Singapore (0.37%) and the Republic of Korea (0.21%) is higher than in other high-income countries with a strong and historical long-standing biomedical sector such as the United Kingdom (0.13%) (WHO Global Observatory on Health R&D).

In economies in Asia and the Pacific with total R&D spending above 0.5% of GDP, the private sector tends to be a major, often the largest, contributor (Table 3.2). For instance, in 2018, businesses funded more than three-quarters of all R&D expenditures in the Republic of Korea (80.5%), Thailand (80.0%), Japan (79.5%), and the PRC (77.5%) (Table 3.2 and section 3.3) (UNESCO 2021; UIS website). However, public funding of R&D is higher than private sector spending on R&D in India and the Islamic Republic of Iran, which are also among the countries spending more than 0.5% of GDP on R&D (UNESCO 2021; UN DESA website; UIS website). While basic and preclinical research previously was
**Figure 3.1: Total Net Official Development Assistance to Medical Research and Basic Health Sectors per Capita ($)**

WHO = World Health Organization.

Note: Data are by recipient country (where available) and for 2019 (or latest year available).


**Figure 3.2: Global Share of Gross Domestic Expenditure in R&D, 2018 (%)**

R&D = research and development.

### Table 3.2: R&D Expenditure as a Share of Gross Domestic Product by Sector of Performance, 2018 (%)

<table>
<thead>
<tr>
<th>Region</th>
<th>Total R&amp;D</th>
<th>Government R&amp;D</th>
<th>Business Enterprise R&amp;D</th>
<th>Private Nonprofit R&amp;D</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Other high-income countries with advanced health and biomedical research sectors</strong></td>
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</tr>
<tr>
<td>Germany</td>
<td>3.00</td>
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<tr>
<td>United Kingdom</td>
<td>1.70</td>
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<td></td>
</tr>
<tr>
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<td><strong>Asia and the Pacific</strong></td>
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<td>0.04(^a)</td>
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</tr>
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<td>0.01</td>
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<td>0.46</td>
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<td>0.01</td>
<td>N/A</td>
</tr>
<tr>
<td>Myanmar</td>
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<td>0.02(^c)</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
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<td>0.27(^c)</td>
<td>0.74(^c)</td>
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<td>0.09(^c)</td>
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<td>N/A</td>
</tr>
<tr>
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<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Philippines</td>
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<td>0.04(^c)</td>
<td>0.06(^c)</td>
<td>N/A</td>
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<tr>
<td>Republic of Korea</td>
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<td>3.64</td>
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<td>Russian Federation</td>
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<td>0.34</td>
<td>0.55</td>
<td>N/A</td>
</tr>
<tr>
<td>Singapore</td>
<td>1.92(^c)</td>
<td>0.21(^c)</td>
<td>1.15(^c)</td>
<td>N/A</td>
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<td>Sri Lanka</td>
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<td>0.05(^c)</td>
<td>0.05(^c)</td>
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<td>Tajikistan</td>
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<td>0.09</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Thailand</td>
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<td>0.05</td>
<td>0.80(^c)</td>
<td>0.01(^c)</td>
</tr>
<tr>
<td>Türkiye</td>
<td>0.95(^c)</td>
<td>0.09(^c)</td>
<td>0.55(^c)</td>
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<td>0.05</td>
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</tr>
<tr>
<td>Viet Nam</td>
<td>0.52(^c)</td>
<td>0.11(^c)</td>
<td>0.38(^c)</td>
<td>0.01(^c)</td>
</tr>
</tbody>
</table>

R&D = research and development.

\(^a\) Data for 2015.
\(^b\) Data for 2016.
\(^c\) Data for 2017.

Note: Data are by economies (where available) and for 2018 unless otherwise indicated.

Sources: United Nations Department of Economic and Social Affairs website and UNESCO Institute for Statistics website.
funded almost exclusively by governments, up to a third of corporate R&D spending in some high-income countries now goes to basic science (UNESCO 2021).

The UNESCO East and Southeast Asia region had 37.6% of the world’s researchers in 2018 (Figure 3.3) (UNESCO 2021; UIS website). The PRC alone accounts for a third of the increase in the global number of researchers between 2014 and 2018 (UNESCO 2021). In 2018, the number of researchers per million inhabitants in full-time equivalents (SDG indicator 9.5.2) in Asia and the Pacific was the highest in the Republic of Korea, Singapore, Japan, and New Zealand, where this indicator was higher than in Germany, the United Kingdom, and the United States (Figure 3.3).

**Figure 3.3: Number of Researchers per Million Inhabitants in Full-Time Equivalents, 2018**

*SDG = Sustainable Development Goal.*

*Note: Data are for 2018 (or latest year available).*

*Sources: UNESCO Institute for Statistics website; UIS.Stat Statistics and Resources website; and World Bank Open Data.*
3.2.2 R&D Output Indicators: Publication, Clinical Trials, and Patents on Vaccines

As of March 2022, Asia and the Pacific carried out 24.1% of all vaccine clinical trials in the world, led by the PRC (with a fifth of all clinical trials of vaccines in Asia and the Pacific and 5.25% in the world), Australia, and the Republic of Korea (Figures 3.4 and 3.5). Many developing countries in the region have also participated in clinical trials. Conducting clinical trials of new vaccines and drugs in developing countries is a significant challenge because of the lack of a research environment, ethical and regulatory hurdles, logistical barriers, and competing demands (Alemayehu, Mitchell, and Nikles 2018). The International Vaccine Institute has supported typhoid and cholera vaccine clinical trials in Nepal and Viet Nam and, as their success attests, carrying out clinical trials in low-income countries can have many positive side effects (Kim and McCann 2021; Saluja et al. 2021): (i) it ensures that vaccine safety and efficacy have been tested in populations of different ethnic and socioeconomic origins, (ii) it not only strengthens research capacities in low-income countries but can also improve the quality of medical care, and (iii) it helps to base R&D and health policy decision-making on locally generated data.

One of the pillars for scientific progress and the eventual translation of basic and preclinical research into new drugs, vaccines, and diagnostic tools is the timely dissemination of scientific results through peer-
reviewed journals.\textsuperscript{1} Since the start of the COVID-19 pandemic, there has been an unprecedented increase in scientific production, in both quantity and speed, on all aspects of the disease, from basic research on the virus to data on clinical trials and therapeutic strategies. Notably, a larger share than usual of articles on COVID-19 has been open access through waivers of subscription fees, open access journals, and public repositories of articles before peer review. The free dissemination of scientific data during the pandemic has been instrumental in improvements in clinical management approaches. As of March 2022, scientists in Asia and the Pacific contributed to a fifth of all scientific publications on vaccine research at all stages—with the PRC, Japan, and India as the largest contributors—on par with figures in the United States (Table 3.3).

\textsuperscript{1} Although the number of open access journals has grown rapidly, 72% of all biomedical research articles require a paid subscription, which creates a barrier to access knowledge for many scientists and doctors in resource-poor countries (Piwowar et al. 2017; Kruesi, Burstein, and Tanner 2020).
### Table 3.3: Number and Share of Scientific Journal Publications on Vaccines

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of Publications</th>
<th>Share of Publications in Asia and the Pacific (%)</th>
<th>Share of World’s Publications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Other high-income countries with advanced health and biomedical research sectors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>World</td>
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<td>100</td>
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<tr>
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<td>3.1</td>
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</tr>
<tr>
<td>United Kingdom</td>
<td>7,693</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>97,978</td>
<td>22.8</td>
<td></td>
</tr>
<tr>
<td>Asia and the Pacific</td>
<td>90,420</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td><strong>Asia and the Pacific</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Afghanistan</td>
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<td>0.02</td>
</tr>
<tr>
<td>American Samoa</td>
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<td>0.00</td>
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<tr>
<td>Armenia</td>
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<tr>
<td>Australia</td>
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<td>0.01</td>
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</tr>
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<td>0.00</td>
</tr>
<tr>
<td>Democratic People’s Rep. of Korea</td>
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<td>0.00</td>
</tr>
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<td>Fiji</td>
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<td>0.01</td>
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<td>French Polynesia</td>
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<td>0.01</td>
<td>0.00</td>
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<td>0.01</td>
<td>0.00</td>
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</tr>
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</table>

*continued on next page*
Table 3.3  continued

<table>
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<tr>
<th>Country</th>
<th>Number of Publications</th>
<th>Share of Publications in Asia and the Pacific (%)</th>
<th>Share of World’s Publications (%)</th>
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<td>0.03</td>
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<td>5</td>
<td>0.01</td>
<td>0.00</td>
</tr>
<tr>
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<td>0.00</td>
</tr>
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<td>0.03</td>
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<td>0.00</td>
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<tr>
<td>Marshall Islands</td>
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<td>0.01</td>
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<td>0.00</td>
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<td>Northern Mariana Islands</td>
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<td>0.00</td>
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<td>Palau</td>
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</table>

continued on next page
Table 3.3 continued

<table>
<thead>
<tr>
<th>Number of Publications</th>
<th>Share of Publications in Asia and the Pacific (%)</th>
<th>Share of World’s Publications (%)</th>
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</tr>
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<td>Timor-Leste</td>
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<td>0.01</td>
</tr>
<tr>
<td>Tonga</td>
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<td>0.00</td>
</tr>
<tr>
<td>Türkiye</td>
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<td>2.34</td>
</tr>
<tr>
<td>Turkmenistan</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Tuvalu</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td>18</td>
<td>0.02</td>
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<td>0.00</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>820</td>
<td>0.91</td>
</tr>
</tbody>
</table>

Note: As of March 2022.
Source: PubMed database.

Research can generate new knowledge, but it does not necessarily generate economic value. For that to happen, R&D must result in the creation of innovative products and processes. An indicator of a country’s ability to innovate is the number of granted patents, which tends to maintain a positive correlation with its R&D spending. In 2019, the PRC, Japan, and the Republic of Korea ranked first, third, and fourth in the world, respectively, in the number of patents filed (WIPO 2022). Other ESCAP countries such as the Russian Federation, India, the Islamic Republic of Iran, and Türkiye stood among the top 15. In the biotechnology and pharmaceutical sectors, the PRC, Japan, and the Republic of Korea have the largest number of patents granted and together have as many as the United States (Table 3.4). According to a 2021 study, 3,660 patents were granted on new countermeasures for coronavirus; notably, 79.8% of the patent holders were from Asia and the Pacific, of which 82.9% were Chinese inventors (Liu et al. 2021).
### Table 3.4: Number of Patents Granted in Biotechnology and Pharmaceuticals in Asia and the Pacific

<table>
<thead>
<tr>
<th>Patents in Biotechnology</th>
<th>Patents in Pharmaceuticals</th>
</tr>
</thead>
<tbody>
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<td><strong>Other high-income countries with advanced health and biomedical research sectors</strong></td>
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</tr>
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<td>World</td>
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</tr>
<tr>
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<td>33,915</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>16,350</td>
</tr>
<tr>
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<td>160,424</td>
</tr>
<tr>
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<td>132,319</td>
</tr>
<tr>
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</tr>
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<td>American Samoa</td>
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<tr>
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</tr>
<tr>
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<tr>
<td>Bangladesh</td>
<td>21</td>
</tr>
<tr>
<td>Bhutan</td>
<td>0</td>
</tr>
<tr>
<td>Brunei Darussalam</td>
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<td>Cambodia</td>
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<td>Fiji</td>
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<td>French Polynesia</td>
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<td>Lao People’s Democratic Republic</td>
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*continued on next page*
Table 3.4  continued

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<tr>
<th>Country</th>
<th>Patents in Biotechnology</th>
<th>Patents in Pharmaceuticals</th>
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<td>Rep. of Korea</td>
<td>24,105</td>
<td>24,724</td>
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<td>Russian Federation</td>
<td>8,679</td>
<td>20,347</td>
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<tr>
<td>Samoa</td>
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<td>Singapore</td>
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<td>Solomon Islands</td>
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<tr>
<td>Sri Lanka</td>
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<td>2</td>
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<tr>
<td>Tajikistan</td>
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<td>73</td>
</tr>
<tr>
<td>Thailand</td>
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<td>47</td>
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<tr>
<td>Timor-Leste</td>
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<td>0</td>
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<td>Tonga</td>
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<td>0</td>
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<td>Türkiye</td>
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<td>539</td>
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<td>Turkmenistan</td>
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<td>7</td>
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<tr>
<td>Tuvalu</td>
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<td>0</td>
</tr>
<tr>
<td>Uzbekistan</td>
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<td>0</td>
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<tr>
<td>Vanuatu</td>
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<tr>
<td>Viet Nam</td>
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</table>

Source: Patentscope website.

### 3.3 Main Actors in Biomedical and Vaccine R&D in Selected Economies in Asia and the Pacific

Many high- and middle-income countries in Asia and the Pacific have specialized research funding government agencies—most often within the organizational structure of the ministries of health, education, or science—that offer grants for early stages of biomedical research (discovery and preclinical stages) at universities and research institutes.

In a large and diverse region like Asia and the Pacific, the vaccine pharmaceutical industry varies greatly by country. Many pharmaceutical companies in high-income Asia and the Pacific are world leaders in vaccine R&D and manufacturing. In several countries in the region, state-owned vaccine manufacturers control a significant share (in some instances, the largest) of the domestic vaccine market and conduct R&D and production of high-quality vaccines, some of which are prequalified by WHO as safe and effective vaccines for purchase by United Nations agencies (Table 3.5). Several state-owned vaccine firms from the region deserve special mention: China National Biotec Group (CNBG), a subsidiary of Sinopharm, accounts for half of the vaccines produced in the PRC and is very active in R&D using both traditional and newer technologies. India has 13 state-controlled (public sector undertakings) pharmaceutical companies, of which at least five (Haffkine Institute, Central Research Institute Kasauli, Pasteur Institute of India, BCG Vaccine Laboratory, and Bharat Immunologicals and Biologicals)
are involved in vaccine R&D and production. In Indonesia, state-owned Biofarma, the country’s only vaccine manufacturer, is engaged in advanced R&D for new vaccines and technologies in partnership with academia. As of March 2022, Biofarma was in talks with WHO to become one of the global manufacturing hubs for mRNA vaccines. Thailand’s state-owned Government Pharmaceutical Organization manufactures vaccines for the domestic market and other countries in the Association of Southeast Asian Nations (ASEAN).

A number of countries in the region have a vibrant **domestically owned private pharmaceutical industry** that not only is involved in vaccine manufacturing but in many cases also conducts its own vaccine R&D (selected private vaccine manufacturers in the region are included in Table 3.5). Of the 41 manufacturers that form the Developing Countries Vaccine Manufacturers Network (DCVMN)—which includes both private and state-owned vaccine producers (see Chapter 2)—34 are based in Asia and the Pacific, most of them private companies. Around half of all WHO-prequalified vaccines are produced by DCVMN manufacturers, of which virtually all (96%) are located in Asia and the Pacific (WHO Prequalification website). As of February 2022, of the 259 presentations for 163 prequalified vaccines, almost two-thirds are developed by manufacturers in Asia and the Pacific (WHO Prequalification website). Vaccine developers across the region have successfully developed vaccine candidates and commercial vaccines for COVID-19 using most of the existing technologies, including new platforms such as viral vector vaccines and several companies in the region are now working toward developing and manufacturing mRNA-based vaccines (Table 3.6).

As the world’s second-largest market for pharmaceuticals, all **multinational pharmaceutical firms** (MNPFs) have a presence in Asia and the Pacific. These firms have not only offshored part of their vaccine and drug manufacturing to Asia and the Pacific but have also transferred some of their R&D activities, directly (to subsidiaries, opening new R&D centers) and/or indirectly (through partnerships with academic institutions or local firms). Most of the largest MNPFs have R&D and manufacturing centers not only in the larger economies (e.g., the PRC, India, Japan, and the Republic of Korea) but also in ASEAN countries. The offshoring of R&D from global vaccine MNPFs to developing countries in Asia and the Pacific can potentially enhance technology transfer to domestic biotechnology firms.
### Table 3.5: Vaccine Companies Involved in R&D in Asia and the Pacific

<table>
<thead>
<tr>
<th>Economy</th>
<th>Company</th>
<th>WHO-Prequalified Vaccines (number)</th>
<th>DCVMN</th>
<th>Private or State-Owned</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>Incepta Vaccine Ltd</td>
<td>No</td>
<td>Yes</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>Beijing Minhai Biotechnology Co., Ltd</td>
<td>No</td>
<td>Yes</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>Beijing Tiant Biological Products Co., Ltd</td>
<td>No</td>
<td>No</td>
<td>State-owned</td>
</tr>
<tr>
<td></td>
<td>BravoVax Co. Ltd</td>
<td>No</td>
<td>Yes</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>Changchun BCHT Biotechnology Co.</td>
<td>No</td>
<td>Yes</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>China National Biotec Group (CNBG)</td>
<td>Yes (2)</td>
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<td>State-owned</td>
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<tr>
<td></td>
<td>Chongqing Zhihe Biomedical Products Co., Ltd</td>
<td>No</td>
<td>Yes</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>Hualan Biological Engineering</td>
<td>Yes (1)</td>
<td>No</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>Institute of Medical Biology Chinese Academy of Medical Sciences</td>
<td>No</td>
<td>Yes</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>Liaoning Cheng Da Biotechnology Co., Ltd.</td>
<td>No</td>
<td>Yes</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>Sinovac Biotech Ltd.</td>
<td>Yes (2)</td>
<td>Yes</td>
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</tr>
<tr>
<td></td>
<td>Walvax Biotechnology Co., Ltd.</td>
<td>No</td>
<td>Yes</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>Xiamen Innovax Biotech Co., Ltd.</td>
<td>Yes (1)</td>
<td>Yes</td>
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</tr>
<tr>
<td>India</td>
<td>Bharat Biotech International Ltd</td>
<td>Yes (10)</td>
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</tr>
<tr>
<td></td>
<td>Bharat Immunologicals and Biologicals Ltd</td>
<td>No</td>
<td>No</td>
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</tr>
<tr>
<td></td>
<td>Biological E. Ltd</td>
<td>Yes (12)</td>
<td>Yes</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>Cadila Pharmaceuticals Ltd</td>
<td>No</td>
<td>No</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>CPL Biologicals Pvt Ltd</td>
<td>No</td>
<td>No</td>
<td>Private</td>
</tr>
<tr>
<td></td>
<td>Green Signal Bio Pharma Pvt Ltd</td>
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</table>

*continued on next page*
### Table 3.5 continued

<table>
<thead>
<tr>
<th>Economy</th>
<th>Company</th>
<th>WHO-Prequalified Vaccines (number)</th>
<th>DCVMN</th>
<th>Private or State-Owned</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haffkine Bio-Pharmaceutical Co. Ltd</td>
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<td>No</td>
<td>State-owned</td>
<td></td>
</tr>
<tr>
<td>Indian Immunologicals Ltd</td>
<td>No</td>
<td>Yes</td>
<td>Private</td>
<td></td>
</tr>
<tr>
<td>Panacea Biotec Ltd</td>
<td>Yes (3)</td>
<td>Yes</td>
<td>Private</td>
<td></td>
</tr>
<tr>
<td>Pasteur Institute of India</td>
<td>No</td>
<td>Yes</td>
<td>State-owned</td>
<td></td>
</tr>
<tr>
<td>Serum Institute of India Ltd</td>
<td>Yes (62)</td>
<td>Yes</td>
<td>Private</td>
<td></td>
</tr>
<tr>
<td>Vins Bioproducts Ltd</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zydus Cadila</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indonesia</td>
<td>PT Bio Farma (Persero)</td>
<td>Yes (15)</td>
<td>Yes</td>
<td>State-owned</td>
</tr>
<tr>
<td>Japan</td>
<td>Astellas Pharma</td>
<td>No</td>
<td>No</td>
<td>Private</td>
</tr>
<tr>
<td>Denka Seiken</td>
<td>No</td>
<td>No</td>
<td>Private</td>
<td></td>
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<tr>
<td>Japan BCG</td>
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<td>Private</td>
<td></td>
</tr>
<tr>
<td>Kaketsuken</td>
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<td>Private</td>
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<tr>
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<td>No</td>
<td>Private</td>
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</tr>
<tr>
<td>Kyoto Biken</td>
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<td>Private</td>
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<tr>
<td>Takeda</td>
<td>No</td>
<td>No</td>
<td>Private</td>
<td></td>
</tr>
<tr>
<td>Korea, Republic of</td>
<td>Boryung Biopharma</td>
<td>No</td>
<td>No</td>
<td>Private</td>
</tr>
<tr>
<td>Cheil Jedant (CJ Pharma)</td>
<td>No</td>
<td>No</td>
<td>Private</td>
<td></td>
</tr>
<tr>
<td>Dong Shin Pharma</td>
<td>No</td>
<td>No</td>
<td>Private</td>
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<tr>
<td>EuBiologics, Co., Ltd.</td>
<td>Yes (2)</td>
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<tr>
<td>GC Pharma</td>
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<td>Yes</td>
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<tr>
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<tr>
<td>LG Life Sciences Ltd</td>
<td>Yes (7)</td>
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<td>Private</td>
<td></td>
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<tr>
<td>SK Bioscience Co., Ltd</td>
<td>Yes (5)</td>
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<td>Pharmianaga Life Sci</td>
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<td>No</td>
<td>Private</td>
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<tr>
<td>Solution Biologics</td>
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<td>No</td>
<td>Private</td>
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<td>Pakistan</td>
<td>Amson Vaccines &amp; Pharma</td>
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<thead>
<tr>
<th>Economy</th>
<th>Company</th>
<th>WHO-Prequalified Vaccines (number)</th>
<th>DCVMN</th>
<th>Private or State-Owned</th>
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<tr>
<td>Russian Federation</td>
<td>Immunopreparat Research productive association, Ufa</td>
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<td>Products Immunologicals and Drugs, Irkutsk RIVS</td>
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<td>No</td>
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<td>LLC Nanolek</td>
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<td>Yes</td>
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<td></td>
<td>St. Petersburg Research Institute of Vaccines and Serums</td>
<td>No</td>
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<td>State-owned</td>
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<td>Taipei, China</td>
<td>Medigen Vaccine Biologicals Co.</td>
<td>No</td>
<td>Yes</td>
<td>Private</td>
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<td>Thailand</td>
<td>BioNet</td>
<td>Yes (1)</td>
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<td></td>
<td>The Government Pharmaceutical Organization</td>
<td>No</td>
<td>Yes</td>
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<td></td>
<td>Queen Saovabha Memorial Institute</td>
<td>No</td>
<td>Yes</td>
<td>State-owned</td>
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<tr>
<td>Viet Nam</td>
<td>The Company of Vaccine and Biological Production No. 1-VABIOTECH</td>
<td>No</td>
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<td>Da Lat Pasteur Vaccines Company Ltd (DAVAC)</td>
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</tr>
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<td></td>
<td>Institute of Vaccines and Medical Biologicals (IVAC)</td>
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<td>No</td>
<td>State-owned</td>
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<td></td>
<td>Center for Research and Production of Vaccines and Biologicals (POLYVAC)</td>
<td>No</td>
<td>Yes</td>
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</tr>
</tbody>
</table>

DCVMN = Developing Countries Vaccine Manufacturers Network, R&D = research and development, WHO = World Health Organization.

Sources: Tsai, Rao, and Xu (2018); DCVMN website; and company websites.
### Table 3.6: Main Types of Vaccine Platforms and Producers of COVID-19 Vaccines in Asia and the Pacific

<table>
<thead>
<tr>
<th>Vaccine Platform</th>
<th>COVID-19 Vaccine Producers in the Region</th>
</tr>
</thead>
</table>
| Live attenuated pathogen | People’s Republic of China: CoronaVac, VeroCell BBIBP-CorV/Sinopharm-Beijing, Sinopharm-Wuhan  
India: BBV152 (Covaxin)  
Islamic Republic of Iran: Shifa Pharmamed vaccine  
Kazakhstan: QazCovid-in  
Russian Federation: CoviVac  
Türkiye: Turkovac |
| Killed pathogen | N/A |
| Toxoid | N/A |
| Subunit (protein, peptide, polysaccharide) | Australia: Spikogen, CpG 1018  
Islamic Republic of Iran and Australia: CinnaGen  
People’s Republic of China: ZF2001/RBD-Dimer, West China Hospital vaccine  
Russian Federation: EpiVacCorona |
| Virus-like protein | N/A |
| Viral vector | People’s Republic of China: Ad5-nCoV/Convidecia  
Russian Federation: Sputnik V |
| Nucleic acid (DNA, RNA) | Several firms in Asia and the Pacific are currently working toward mRNA vaccines for COVID-19. |
| Antigen-presenting cells (dendritic cells), T cells | N/A |
| Bacterial vector | N/A |

N/A = not available as of March 2022.

Sources: Iwasaki and Omer (2020) and Pollard and Bijker (2021).

In developed countries, stricter ethical standards and regulatory environments make conducting clinical trials more difficult and expensive. As a result, MNPFs have outsourced various stages of vaccine and drug R&D to **contract research organizations (CROs)** with a presence in developing countries (Sayed and Agndal 2022). Nevertheless, weaker and more unpredictable regulatory environments in developing countries can also be an obstacle to the offshoring of clinical trials and R&D. All global CROs now have a presence in Asia and the Pacific, particularly in India, the PRC, and Japan, and also carried out early stages of R&D at their locations in Asia and the Pacific. Dozens of domestically owned CROs have emerged in the region, especially the PRC and India, and some CROs in the region have gained global reach; for instance, the Chinese CRO WuXi AppTec Group ranked eighth in the world based on revenue in 2020/21 (Vietchinkina 2022).
3.4 R&D Preparedness and the Vaccine R&D Pipeline in Asia and the Pacific

In most countries of the world, national preparedness plans to deal with epidemics and pandemics have focused primarily on influenza. Still, 99 countries have no preparedness plans for influenza outbreaks (Nuzzo et al. 2019; WHO SPH Portal), of which 13 are in Asia and the Pacific: Afghanistan, Armenia, the Democratic People’s Republic of Korea, the Islamic Republic of Iran, Kazakhstan, the Kyrgyz Republic, Nepal, Pakistan, the Russian Federation, Tajikistan, Türkiye, Turkmenistan, and Uzbekistan (WHO SPH Portal).

Many of the vaccines currently used not only in Asia and the Pacific but also around the world have been researched, developed, and/or manufactured by the larger pharmaceutical firms in the region, especially in Japan, the PRC, India, and Australia, and also in smaller economies like Viet Nam. Some developing countries in Asia and the Pacific that until recently only hosted vaccine fill-and-finish manufacturing operations are now also engaged in vaccine R&D for new vaccines. Vaccines researched and developed in Asia and the Pacific for diseases of regional importance include those for severe acute respiratory syndrome (SARS), Japanese encephalitis, the Hantaan and Seoul viruses that cause hemorrhagic fever with renal syndrome, Russian spring–summer encephalitis, Kyasanur forest disease, cholera, and Q fever (Tsai, Rao, and Xu 2018). Manufacturers in Asia and the Pacific have also developed for national or regional distribution newer vaccines for measles, mumps, hepatitis A, rotavirus, and intranasally delivered vaccines for pandemic H1N1 virus. Some new vaccines developed in the region have been distributed globally such as those for hepatitis E, enterovirus A71, and COVID-19 (Tsai, Rao, and Xu 2018).

As of December 2021, the vaccine R&D pipeline in Asia and the Pacific includes new vaccines for tuberculosis, malaria, HIV, kinetoplastids (e.g., Chagas disease, sleeping sickness, leishmaniasis), diarrheal diseases, hepatitis C, Salmonella, bacterial pneumonia and meningitis, rheumatic fever, and COVID-19 (Table 3.7). In fact, 100% of the world’s new vaccine candidates for Salmonella, 66.8% for bacterial pneumonia and meningitis, 43.8% for tuberculosis, and 36.8% for

---

2 When technological and/or manufacturing capacities are limited or when production volumes are small, vaccine manufacturers do not conduct upstream stages of vaccine manufacturing (e.g., bioprocessing and formulation), but rather limit their activity to downstream steps where the vaccines are filled into vials and packaged for distribution (fill, finish, and packaging).
From Lab to Jab: Improving Asia and the Pacific’s Readiness to Produce and Deliver Vaccines

diarrheal diseases are being researched and developed in Asia and the Pacific (Table 3.7 and Policy Cures Research R&D Pipeline Tracker website). Several countries in the region have been at the forefront of R&D for COVID-19 (Table 3.5). Notably, clinical trials of the PRC’s CanSino Biologics COVID-19 vaccine started in March 2020, at the same time as Moderna’s clinical trials in the United States (Chakraborty et al. 2021).

Table 3.7: Vaccine Candidates in the Pipeline of Firms in Asia and the Pacific

<table>
<thead>
<tr>
<th>Disease</th>
<th>R&amp;D Stage</th>
<th>Vaccine Candidate</th>
<th>Pharmaceutical Firm/ Research Institute</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>Preclinical</td>
<td>CysVac2/A</td>
<td>Tuberculosis Vaccine Initiative and University of Sydney</td>
<td>International Australia</td>
</tr>
<tr>
<td></td>
<td>Phase I</td>
<td>Ad5Ag85A</td>
<td>CanSino Biologics Inc.</td>
<td>PRC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>McMaster University</td>
<td>Canada</td>
</tr>
<tr>
<td></td>
<td>Phase II</td>
<td>AEC/BCO2</td>
<td>Anhui Zhifei Longcom Biopharmaceutical Co. Ltd</td>
<td>PRC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GamTBVac</td>
<td>Gamaleya Research Institute of Epidemiology and Microbiology</td>
<td>Russian Federation</td>
</tr>
<tr>
<td></td>
<td>Phase III</td>
<td>TB-FLU-04L</td>
<td>Kazakhstan Ministry of Health Research Institute for Biological Safety Problems</td>
<td>Kazakhstan</td>
</tr>
<tr>
<td></td>
<td>MIP</td>
<td>VMP1002</td>
<td>Serum Institute of India</td>
<td>India</td>
</tr>
<tr>
<td></td>
<td>Vaccae</td>
<td></td>
<td>Anhui Zhifei Longcom Biopharmaceutical Co. Ltd and Institute of Microbiology, Chinese Academy of Sciences</td>
<td>PRC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vakzine Projekt Management GmbH</td>
<td>Germany</td>
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<table>
<thead>
<tr>
<th>Disease</th>
<th>R&amp;D Stage</th>
<th>Vaccine Candidate</th>
<th>Pharmaceutical Firm/ Research Institute</th>
<th>Country</th>
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<tr>
<td>Malaria</td>
<td>Preclinical</td>
<td>Pfs230 fragments</td>
<td>Ehime University and PATH</td>
<td>Japan International</td>
</tr>
<tr>
<td></td>
<td>Phase I</td>
<td>ChAd63/MVA PvDBP</td>
<td>International Centre for Genetic Engineering</td>
<td>India</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Biotechnology and Okairos</td>
<td>Switzerland</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PlasprotecT</td>
<td>Griffith University</td>
<td>Australia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PvDBPII</td>
<td>Syngene International Limited</td>
<td>India</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>International Centre for Genetic Engineering and Biotechnology</td>
<td></td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Phase I</td>
<td>5eV-G (NP), Ad35-GRIN</td>
<td>DNAVEC Corporation</td>
<td>Japan</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>International AIDS Vaccine Initiative</td>
<td>International</td>
</tr>
<tr>
<td></td>
<td>Phase II</td>
<td>HIV DNA-rTV</td>
<td>Beijing Bioproduct Research Institute and Beijing You Ann Hospitals</td>
<td>PRC</td>
</tr>
<tr>
<td>Kinetoplastids</td>
<td>Preclinical</td>
<td>LmCen-/-</td>
<td>Gennova Biopharmaceuticals</td>
<td>India</td>
</tr>
<tr>
<td>(Chagas disease, sleeping sickness, leishmaniasis)</td>
<td></td>
<td></td>
<td>McGill University</td>
<td>Canada</td>
</tr>
<tr>
<td></td>
<td>Phase I</td>
<td>LEISH-F3+GLA-SE</td>
<td>Gennova Biopharmaceuticals</td>
<td>India</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Infectious Disease Research Institute</td>
<td>US</td>
</tr>
<tr>
<td>Diarrheal diseases</td>
<td>Preclinical</td>
<td>34kDa OMP</td>
<td>Indian National Institute of Cholera and Enteric Diseases</td>
<td>India</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Indian National Institute of Cholera and Enteric Diseases</td>
<td>India</td>
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### Table 3.7 continued

<table>
<thead>
<tr>
<th>Disease</th>
<th>R&amp;D Stage</th>
<th>Vaccine Candidate</th>
<th>Pharmaceutical Firm/ Research Institute</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hexavalent BRV vaccine</strong></td>
<td>Phase I</td>
<td>Wuhan Institute of Biological Products Co Ltd and Hebei Province Center for Disease Prevention and Control</td>
<td>PRC</td>
<td></td>
</tr>
<tr>
<td><strong>S. Flexneriza–S. Sonei bivalent conjugate vaccine</strong></td>
<td></td>
<td>Beijing Zhifei Lanzhou Biopharmaceutical Co. Ltd.</td>
<td>PRC</td>
<td></td>
</tr>
<tr>
<td><strong>VLP VP2/6/7</strong></td>
<td></td>
<td>Mitsubishi Tanabe Pharma Corporation</td>
<td>Japan</td>
<td></td>
</tr>
<tr>
<td><strong>Heat stable rotavirus (HSRV) vaccine</strong></td>
<td>Phase II</td>
<td>Hilleman Laboratories</td>
<td>India</td>
<td></td>
</tr>
<tr>
<td><strong>RV3-BB</strong></td>
<td></td>
<td>MSD (Merck)</td>
<td>Germany</td>
<td></td>
</tr>
<tr>
<td><strong>BRV-TV</strong></td>
<td>Phase III</td>
<td>Shantha Biotechnics (Sanofi Group)</td>
<td>India</td>
<td></td>
</tr>
<tr>
<td><strong>P2-VP8-P[8]</strong></td>
<td></td>
<td>SK Chemicals</td>
<td>ROK</td>
<td></td>
</tr>
<tr>
<td><strong>PATH</strong></td>
<td></td>
<td></td>
<td>International</td>
<td></td>
</tr>
<tr>
<td><strong>Hepatitis C</strong></td>
<td>Preclinical</td>
<td>HepSeeVax</td>
<td>Burnet Institute</td>
<td>Australia</td>
</tr>
<tr>
<td><strong>Salmonella</strong></td>
<td>Preclinical</td>
<td>OSP-rEPA</td>
<td>Abasyn University</td>
<td>Pakistan</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Canadian National Research Council</td>
<td>Canada</td>
<td></td>
</tr>
<tr>
<td><strong>Trivalent typhoid/iNTS glycoconjugate vaccine</strong></td>
<td></td>
<td>Bharat Biotech University of Maryland, Baltimore</td>
<td>India US</td>
<td></td>
</tr>
<tr>
<td><strong>Vi-CRM197+O:2-CRM197</strong></td>
<td></td>
<td>Biological E. Limited Novartis Vaccine Institute for Global Health</td>
<td>India Switzerland</td>
<td></td>
</tr>
<tr>
<td><strong>Live oral PA vaccine (CVD 1902)</strong></td>
<td>Phase I</td>
<td>Bharat Biotech University of Maryland, Baltimore</td>
<td>India US</td>
<td></td>
</tr>
</tbody>
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## Table 3.7 continued

<table>
<thead>
<tr>
<th>Disease</th>
<th>R&amp;D Stage</th>
<th>Vaccine Candidate</th>
<th>Pharmaceutical Firm/ Research Institute</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase II</strong></td>
<td>O:2-TT</td>
<td>Lanzhou Institute of Biological Products</td>
<td>PRC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>US National Institutes of Health</td>
<td>US</td>
<td></td>
</tr>
<tr>
<td>Vi-CRM197</td>
<td>Biological E. Limited</td>
<td>Novartis Vaccine Institute for Global Health</td>
<td>PRC</td>
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<tr>
<td></td>
<td></td>
<td>Switzerland</td>
<td></td>
<td></td>
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<tr>
<td>Vi-DT</td>
<td>Biofarma</td>
<td>SK Chemicals</td>
<td>ROK</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Indonesia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vi-rEPA</td>
<td>Lanzhou Institute of Biological Products</td>
<td>United States National Institutes of Health</td>
<td>PRC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>US</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterial pneumonia and meningitis</td>
<td>Preclinical</td>
<td>23-valent pneumococcal PS vaccine</td>
<td>Sinovac Biotech Ltd</td>
<td>PRC</td>
</tr>
<tr>
<td></td>
<td>A, C, Y, W135 meningococcal PS conjugate vaccine</td>
<td>China Air Force Medical University and Chinese National Institute for Food and Drug Control</td>
<td>PRC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ASP3772</td>
<td>Astellas Pharma</td>
<td>Japan</td>
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<tr>
<td></td>
<td></td>
<td>Affinivax</td>
<td>US</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GBP411</td>
<td>SK Chemicals</td>
<td>ROK</td>
<td></td>
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<td></td>
<td></td>
<td>Sanofi</td>
<td>France</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tetravalent meningococcal conjugate vaccine</td>
<td>Wuhan Institute of Biological Products and Lanzhou Institute of Biological Products</td>
<td>PRC</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase II</td>
<td>Biological E 14-valent PCV</td>
<td>Biological E Ltd</td>
<td>India</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LBVE013 (multivalent)</td>
<td>LG Life Sci</td>
<td>ROK</td>
<td></td>
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<tr>
<td></td>
<td>Pentavalent meningococcal conjugate vaccines</td>
<td>Serum Institute of India</td>
<td>India</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PATH</td>
<td>International</td>
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Table 3.7 continued

<table>
<thead>
<tr>
<th>Disease</th>
<th>R&amp;D Stage</th>
<th>Vaccine Candidate</th>
<th>Pharmaceutical Firm/Research Institute</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatic fever</td>
<td>Phase III</td>
<td>MCV4</td>
<td>CanSino Biologics Inc.</td>
<td>PRC</td>
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<tr>
<td></td>
<td></td>
<td>MCV-ACYW135</td>
<td>Beijing Minhai Biotechnology</td>
<td>PRC</td>
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<tr>
<td></td>
<td></td>
<td>NBP606</td>
<td>SK Chemicals</td>
<td>ROK</td>
</tr>
<tr>
<td></td>
<td>Phase I</td>
<td>MJ8VAX (J8-DT)</td>
<td>Australian Centre for Health Services Innovation and Q-Pharm</td>
<td>Australia</td>
</tr>
</tbody>
</table>


Sources: Policy Cures Research R&D Pipeline Tracker website and email communications with individual companies.

3.5 National Strategies for Incentivizing Investment and Partnerships in Vaccine R&D

Countries in Asia and the Pacific have used several of the supply- and demand-side approaches (described in Chapter 2) to incentivize investments in vaccine R&D and manufacturing by pharmaceutical firms.

3.5.1 Supply-Side Approaches

On the supply side, many governments in the region offer grants to universities and research institutes to carry out early stages of biomedical R&D (Table 3.8). In 2013, the Australian National Health and Medical Research Council ranked seventh and the National Natural Science Foundation of China (NNSF-China) ninth among the world’s top 10 public funders of biomedical and health research. Reflecting the rapid growth in biomedical and health R&D expenditures and the number of researchers in Asia and the Pacific, by 2021, the NNSF-China, the Japan Science and Technology Agency, and the National Research
Foundation of Korea respectively ranked second, third, and fourth in the world for funds disbursed. However, beyond funding for R&D in COVID-19 vaccines, the share of public funding for health R&D that countries in Asia and the Pacific earmark for vaccine R&D is either unavailable or only fragmentary, especially in middle- and low-income countries. As part of its $5.2 billion science and technology budget for 2021, the Republic of Korea spent $37 million on developing new vaccines and drugs for emerging infectious diseases (Sharma 2021).

Table 3.8: Government Agencies Funding Health and Biomedical R&D in Asia and the Pacific

<table>
<thead>
<tr>
<th>Funding Agency</th>
<th>Country</th>
<th>Value in $ (date)</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outside Asia and the Pacific (included in the world’s top 10)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congressionally Directed Medical Research Programs (CDMRP) - Department of Defense</td>
<td>United States</td>
<td>1.3 billion (2020)</td>
<td><a href="https://cdmrp.army.mil/default">https://cdmrp.army.mil/default</a></td>
</tr>
<tr>
<td>Medical Research Council</td>
<td>United Kingdom</td>
<td>1.1 billion (2021)</td>
<td><a href="https://mrc.ukri.org/">https://mrc.ukri.org/</a></td>
</tr>
<tr>
<td><strong>Asia and the Pacific</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National Research Foundation of Korea</td>
<td>ROK</td>
<td>2.0 billion (2021)</td>
<td><a href="https://www.nrf.re.kr/eng/index">https://www.nrf.re.kr/eng/index</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>497.7 million (2020)</td>
<td></td>
</tr>
</tbody>
</table>
Table 3.8  continued

<table>
<thead>
<tr>
<th>Funding Agency</th>
<th>Country</th>
<th>Value in $ (date)</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indian Council of Medical Research</td>
<td>India</td>
<td>140.3 million (2013)</td>
<td><a href="https://www.icmr.gov.in/index.html">https://www.icmr.gov.in/index.html</a></td>
</tr>
<tr>
<td>Russian Foundation for Basic Research</td>
<td>Russian Federation</td>
<td>N/A</td>
<td><a href="https://www.rfbr.ru/rffi/eng">https://www.rfbr.ru/rffi/eng</a></td>
</tr>
<tr>
<td>Biomedical Research Council of the Agency for Science, Technology and Research</td>
<td>Singapore</td>
<td>N/A</td>
<td><a href="https://www.a-star.edu.sg/">https://www.a-star.edu.sg/</a></td>
</tr>
<tr>
<td>Ministry of Science and Technology of the PRC</td>
<td>PRC</td>
<td>N/A</td>
<td><a href="http://en.most.gov.cn/">http://en.most.gov.cn/</a></td>
</tr>
<tr>
<td>Department of Biotechnology</td>
<td>India</td>
<td>N/A</td>
<td><a href="https://dbtindia.gov.in/">https://dbtindia.gov.in/</a></td>
</tr>
<tr>
<td>Department of Science and Technology</td>
<td>India</td>
<td>N/A</td>
<td><a href="https://dst.gov.in/">https://dst.gov.in/</a></td>
</tr>
<tr>
<td>Indonesian Institute of Sciences (LIPI)</td>
<td>Indonesia</td>
<td>N/A</td>
<td><a href="http://lipi.go.id/">http://lipi.go.id/</a></td>
</tr>
<tr>
<td>Scientific and Technological Research Council of Türkiye (TÜBİTAK)</td>
<td>Türkiye</td>
<td>N/A</td>
<td><a href="https://www.tubitak.gov.tr/en">https://www.tubitak.gov.tr/en</a></td>
</tr>
<tr>
<td>Turkish Academy of Sciences (TÜBA)</td>
<td>Türkiye</td>
<td>N/A</td>
<td><a href="http://www.tuba.gov.tr/">http://www.tuba.gov.tr/</a></td>
</tr>
</tbody>
</table>

N/A = not available, PRC = People’s Republic of China, R&D = research and development, ROK = Republic of Korea.

Sources: Websites of funding agencies; Viergever and Hendriks (2016); and Aars, Clark, and Schwalbe (2021).
Product development partnerships (PDPs) and non-PDP intermediaries are, together with governments, among the main sources of funding for the R&D of vaccines on neglected and/or emerging infectious diseases. As in the case of public funding, data on the share of R&D expenditures funded by philanthropic foundations in Asia and the Pacific are incomplete. Most PDPs and non-PDP intermediaries, as well as global philanthropic foundations, have funded projects for vaccine and drug R&D in developing countries in Asia and the Pacific. In total, 20 ESCAP members have benefited from vaccines for infectious diseases purchased by Gavi, the Vaccine Alliance (Gavi website). The Coalition for Epidemic Preparedness Innovations (CEPI) has created economic incentives to bring vaccine candidates from the discovery to the end of Phase II for various regionally prevalent diseases such as those caused by chikungunya and Nipah viruses. Governments in several high-income countries in Asia and the Pacific are major contributors to PDP and non-PDP intermediaries and philanthropic foundations. During 2017–2019, the Governments of Japan and Australia were among the world’s top 10 donors to PDP and non-PDP intermediaries that funded vaccine and drug R&D for emerging infectious diseases (PCR 2021a). The Japanese government is also the largest contributor to the Global Health Innovative Technology (GHIT) Fund, a non-PDP intermediary that, in collaboration with the Bill & Melinda Gates Foundation, the Wellcome Trust, and the United Nations Development Programme, mobilizes the Japanese pharmaceutical industry, academia, and research institutes to create new vaccines, drugs, and diagnostics for malaria, tuberculosis, and neglected tropical diseases (PCR 2021b).

As noted earlier, public spending in R&D encourages investment by the private sector (David, Hall, and Toole 2000). Nevertheless, a survey in 53 countries around the world found that most pharmaceutical firms have relatively low interest in establishing R&D collaborations with universities (UNESCO 2021). The survey revealed that most firms—both in developed and developing countries—prefer to maintain their core R&D activities in-house rather than outsource them to academic researchers (UNESCO 2015). Less than 2% of scientific publications in New Zealand and the PRC involved coauthorship between universities and businesses. In the Republic of Korea, academia–business coauthorship was higher (3.9%) and more similar to the levels found in Germany (4.4%) and France (4.5%) (UNESCO 2021). To promote knowledge transfer and accelerate innovation, many government agencies in Asia and the Pacific, including some in developing countries, have programs to boost university–industry R&D ties and offer funds or provide tax incentives for firms that finance some of the total cost
of a project (DOST Philippines 2021; UNESCO 2021). In Pakistan, the World Bank has supported a fund that offers grants for collaborations between academic researchers and businesses when the latter match government funding (HEC 2021).

3.5.2 Demand-Side Approaches

The impact of demand-side strategies to incentivize vaccine R&D depends on the type of vaccines and the structure of the pharmaceutical industry. In many developing countries, vaccines included in national immunization programs are researched, developed, and manufactured by state-owned pharmaceutical firms that supply most of the doses needed. In developing countries where private firms also conduct R&D and manufacturing for vaccines in national immunization programs, demand-side approaches can incentivize local private pharmaceutical firms to invest in vaccine R&D. However, in the case of vaccines for neglected infectious diseases and in countries without vaccine R&D and manufacturing capacity that rely on imported vaccines, demand-side approaches by governments may have only limited effects on the structure of economic incentive structure for pharmaceutical firms abroad, especially for MNPFs.

Governments can create demand for vaccines through free vaccination, incentives for people to get vaccinated, or mandatory vaccination in schools or the workplace. In most countries in the region, governments provide the vaccines administered in national immunization programs and those required during epidemics and pandemics free of charge. Legislation on vaccination varies across Asia and the Pacific. Several countries in the region have compulsory vaccination for their national immunization programs and/or for school enrollment, although many low-income countries have limited capacity to implement (e.g., supply, delivery, and access issues) and enforce these programs (Vanderslott and Marks 2021). In addition, there is still an open debate on whether mandatory vaccination is the best way to achieve high uptake. Japan, New Zealand, and the Republic of Korea previously had mandatory childhood immunization schedules but were later superseded by voluntary vaccination along with strong recommendations. Australia offers tax incentives and childcare benefits for parents who vaccinate their children.

As discussed in Chapter 2, advanced purchase agreements (APAs) have been successfully used to incentivize investment by pharmaceutical firms in vaccine R&D and manufacturing. APAs are part of pandemic influenza preparedness plans with signatory countries paying an annual fee to the manufacturer and committing
to purchase a specified number of annual doses (Turner 2016). Before the COVID-19 pandemic, in Asia and the Pacific, only high-income countries had used APAs (Turner 2016; Pharmaceutical Technology 2021). For instance, during the 2009 H1N1 pandemic, New Zealand was the only country in Asia and the Pacific that held an APA for H1N1 vaccines. If vaccine supply is inelastic, APAs between high-income countries with pharmaceuticals can lead to higher prices and negative externalities for low-income countries. However, APAs can also foster global capacity expansion and accelerate R&D and manufacturing, creating positive externalities for third countries (Ahuja et al. 2021).

To ensure equity in vaccine supply, WHO encourages developing countries to use APAs and some MNPFs like GSK have pledged to supply vaccines to developing countries via APAs at tiered prices based on the country’s GDP (WHO 2011; Turner 2016).

During the COVID-19 pandemic, pharmaceutical firms in Asia and the Pacific signed APAs with the COVID-19 Vaccines Global Access (COVAX) facility, including the Gamaleya Institute (Russian Federation), Sinovac (PRC), CanSino Biologics (PRC), Bharat Biotech (India), and the Serum Institute of India (India) (Pharmaceutical Technology 2021). As part of COVAX, Gavi has established advanced market commitments (AMCs) by pooling up to $2.4 billion from the financial contributions of high-income countries to support R&D and manufacturing for several COVID-19 vaccines before they have been approved (Phelan et al. 2020). Thirteen ESCAP members have signed self-financing agreements with the COVAX AMC: Armenia, Australia, Azerbaijan, Brunei Darussalam, Georgia, the Islamic Republic of Iran, Japan, Nauru, New Zealand, Palau, the PRC, the Republic of Korea, and Singapore. In addition, 30 ESCAP members are among the 92 lower-income economies eligible to benefit from the COVAX AMC with vaccine doses paid through official development assistance and contributions from the private sector and philanthropy (Gavi website).

### 3.6 Regional Cooperation in Vaccine R&D

The advantages of regional cooperation in epidemic surveillance and health care during an epidemic or pandemic are obvious. It helps contain the spread of disease and optimize the utilization of medical infrastructure and supplies within the region. This is particularly important for developing countries with weak health systems and limited resources. Countries can also cooperate in vaccine R&D in several ways, from informal cooperation between scientists in joint R&D projects to the coordination of activities among all stakeholders—governments, regional intergovernmental organizations, or region-wide
private associations—in the pooling of R&D funding or the prioritization of diseases for vaccine R&D pipelines.

The COVID-19 pandemic has highlighted the possibilities of international cooperation but also its potential fragility. On the one hand, the pandemic has made evident how beggar-thy-neighbor policies with export restrictions on medical personal protective equipment and vaccines can impact the production networks of these products. Vaccine nationalism already took place during the H1N1 epidemic and has reemerged during the COVID-19 pandemic. These inward-looking strategies are not an option for many middle- and low-income countries that depend on the vaccines produced elsewhere. Likewise, attempts to waive intellectual property rights on COVID-19 vaccines have been blocked by pharmaceutical firms that own them. On the other hand, the pandemic has shown that cooperation between actors (governments, firms, nonprofit sector) across Asia and the Pacific and beyond was essential for accelerating the timeline of COVID-19 vaccine development (Chakraborty et al. 2021). International cooperation in R&D during the COVID-19 pandemic was in part possible due to previously existing informal networks and formal institutional linkages between actors. For instance, there was sharing of data and knowledge by the scientific community, international PDPs, and other non-PDP intermediaries, channeling of funding from governments and philanthropic foundations to companies and institutes capable of developing vaccines, and international organizations and regional intergovernmental associations coordinating the activities of public and private actors. Organizations like CEPI and Gavi that existed before the pandemic pulled together with WHO to create COVAX (COVID-19 Vaccines Global Access) to accelerate R&D and production of vaccines for COVID-19.

Pharmaceutical firms in developing countries can build their vaccine R&D capabilities through technological transfer from PDPs and/or pharmaceutical firms from high-income countries. Pharmaceutical firms in developing countries have also gained technological expertise through South–South cooperation and South–South Triangular Cooperation (SSTC). For instance, SSTC was used to carry out R&D when the Nepal Health Research Council conducted Phase III clinical trials in Nepal for a new typhoid conjugate vaccine, with help from the International Vaccine Institute, SK Bioscience (Republic of Korea), and Biofarma (Indonesia) and with funding from the Bill & Melinda Gates Foundation and International Vaccine Institute member states (Kim and McCann 2021; Saluja et al. 2021). Another successful example of SSTC in vaccine R&D was the oral cholera vaccines developed between Santha Biotechnics (India), VABIOTECH (Viet Nam), and EuBiologics (Republic of Korea) (WHO 2017; Odevall et al. 2018).
Regional institutions and intergovernmental organizations can help promote and coordinate regional cooperation. Amaya and De Lombaerde (2021) outlined several functions that intergovernmental organizations can play in the context of health emergencies. First, they can bridge global and national levels: vertically, by translating global agreements to national policies and targets, and horizontally, by supporting and coordinating actions by countries in addressing cross-border policy challenges. Second, intergovernmental organizations can facilitate the cross-border mobilization of medical supplies, vaccines, and their intermediates, encouraging maintaining open borders for the trade of goods while controlling the spread of the disease. Third, intergovernmental organizations can facilitate the joint procurement of medical supplies, drugs, and vaccines through pooled purchasing, ensuring a lower price for low-income countries. Finally, intergovernmental organizations can also coordinate the work of donors and partners to support countries.

During the SARS epidemic, the ASEAN Secretariat issued recommendations and supported members in their responses to contain its spread, a strategy that WHO commended (Amaya and De Lombaerde 2021). The Permanent Committee on Science, Technology and Innovation was established by ASEAN to promote cooperation in science, technology, and innovation (ST&I) among ASEAN members and to raise the level of scientific and technological advancement in member states. The ASEAN Plan of Action on Science, Technology, and Innovation (APASTI) 2016–2025 aims, among other things, to intensify R&D collaboration between the public and private sectors to address common problems in ASEAN, develop ST&I human resources, create a network of ST&I centers of excellence across the region, strengthen ST&I infrastructure, and create closer cooperation in R&D with ASEAN dialogue partners (Australia, Canada, the European Union, India, Japan, New Zealand, the PRC, the Republic of Korea, the Russian Federation, and the United States) (ASEAN 2017). In April 2020, the United States launched the US–ASEAN Health Futures initiative to strengthen public health in ASEAN through R&D, health system capacity, and the development of human capital in health. In the first area, joint R&D in ASEAN includes more than 300 active joint research projects between ASEAN members and more than 20 of the US National Institutes of Health, over $30 million in research grants to universities and government research institutions in ASEAN, and support for clinical trials of treatments of infectious diseases (US–ASEAN 2020). ASEAN had a very active profile during the COVID-19 pandemic with at least 11 new health initiatives, including establishing the ASEAN Centre for Public Health Emergencies and Emerging Diseases to manage and coordinate
resources in health response and the ASEAN Public Health Emergency Coordination System to improve and harmonize preparedness for and response to health emergencies. The United States and the European Union donated doses of COVID-19 vaccines to low- and middle-income ASEAN countries through COVAX (ASEAN 2021; US Department of State 2021). The United States Centers for Disease Control and Prevention has established the US–ASEAN Infection Prevention and Control Task Force. The South Asian Association for Regional Cooperation (SAARC), which has had relatively little activity in health and biomedical research, during the COVID-19 pandemic created a health emergency fund of $18 million to pool human resources and supplies and share knowledge (ESCAP 2020; LSE 2021). In addition to sharing medical supplies, SAARC countries planned to create mechanisms for coordinating R&D activities and disease surveillance. The World Bank lauded SAARC’s short-term collaboration on COVID-19 for its potential longer-term spillovers to increase regional integration (LSE 2021). ESCAP can act as a catalyst for these types of collaborative R&D initiatives in Asia and the Pacific at the regional level by bringing together all stakeholders—member states, subregional organizations such as ASEAN or SAARC, multilateral development banks, companies, philanthropic foundations, and civil society—and harnessing its substantive and management expertise in regional cooperation.

Regional collaboration on R&D can also be channeled and coordinated through scientific associations and research networks. The Association of Academies and Societies of Sciences in Asia (AASSA) was constituted in 2012 as a nonprofit organization that encompasses 32 scientific and technological academies and science societies from 30 countries in Asia and the Pacific. AASSA organizes seminars and publishes reports on ST&I issues. However, the association’s activity has been relatively low compared to counterparts in other regions. For instance, in the context of COVID-19, AASSA held a 1-day webinar aimed at identifying the key activities and recommendations of member academies in response to the pandemic. In comparison, the African Academy of Sciences has a wide range of activities, such as funding scholarships and research grants, strengthening R&D infrastructure in research institutes across Africa, fostering and funding joint R&D projects and networks between African scientists, and establishing partnerships with leading scientific organizations and research funding agencies for capacity.

In the past 2 decades, several regional and subregional research networks connecting research institutions across Asia and the Pacific have been established. Although they can play important roles in promoting vaccine R&D in the region, some of these initiatives
have exhibited relatively low levels of activity since their creation. At the subregional level, the South East Asia Infectious Disease Clinical Research Network (SEAICRN) facilitates clinical research collaborations between hospitals and research institutions in Thailand, Viet Nam, and Indonesia (SEAICRN website). The WHO Regional Office for South-East Asia (2003) has proposed the creation of regional vaccine research networks that bring together governments, research institutions, manufacturers (including firms in the DCVMN), and WHO to promote information sharing and regional R&D and to address ethical guidelines and intellectual property rights issues. It is also worth highlighting the ASEAN Network for Drugs, Diagnostics, Vaccines and Traditional Medicines Innovation (ASEAN-NDI), which was launched in 2010 (ASEAN-NDI website). Other initiatives are disease specific; for instance, the AIDS Vaccine for Asia Network (AVAN) was launched in 2011 to facilitate the development of a regional strategy that accelerates R&D of an HIV/AIDS vaccine through government advocacy, improved coordination, and harmonization of research; develops clinical trial and manufacturing capacity; supports ethical and regulatory frameworks; and ensures community participation.

### 3.7 Strengthening Domestic and Regional Partnerships among Actors in Vaccine R&D

In all countries, regardless of their level of development and/or geographical location, the transfer of knowledge from academia to the pharmaceutical industry faces constraints. Governments can promote academia-industry ties through interrelated policies and regulations, several of them already implemented in Asia and the Pacific, including (i) provide funding for joint university-private sector projects; (ii) promote financial management rules of universities to foster university-industry partnerships; (iii) better define intellectual property rights for researchers and institutions funded by public grants and protect the intellectual property rights of pharmaceutical firms and academic institution in the context of knowledge sharing and technology transfer; (iv) promote greater flexibility in universities to allow academic researchers to conduct projects in pharmaceutical companies; (v) establish business incubators at universities; and (vi) facilitate the membership of academic researchers to participate in boards of companies and of industry leaders in university committees.

Partnerships between scientists in Asia and the Pacific should be encouraged, facilitated, and, when possible, funded. Most often, scientists, universities, and research institutes share scientific
knowledge and data across countries through informal networks. Although institutionalizing these informal networks may not necessarily improve scientific collaboration, national governments, intergovernmental organizations, and scientific societies can promote it by offering travel grants for scientific meetings and research grants for international collaborative R&D projects. Creating regional and subregional vaccine research networks can bring together WHO, national governments, research institutions, and the private sector to promote sharing of data and knowledge for vaccine R&D, and these networks can serve as platforms for advocacy, establishing research priorities, promoting joint projects, and coordinating funding initiatives. Existing scientific societies and research networks should increase their activities and expand their goals to promote joint R&D projects, fellowships, and exchanges of scientists between research institutes in Asia and the Pacific.

**Intergovernmental organizations** in Asia and the Pacific can play a more active role in coordinating the policies and actions in vaccine R&D. They can map regional and subregional needs and elaborate, in collaboration with WHO regional offices and other stakeholders, R&D action plans for prioritized diseases. They can also promote the sharing of scientific knowledge and data, helping to coordinate the division of labor in vaccine R&D among countries according to the strengths and weaknesses of each country. WHO can provide technical support to regional and subregional intergovernmental organizations in these tasks. Intergovernmental organizations in Asia and the Pacific can also play a key role in advocacy for R&D for vaccines and drugs at the global level.

One policy option is to establish a **regional (or subregional) R&D funding agency** in Asia and the Pacific focused on infectious diseases of regional importance which offers grants for research projects and fellowships for capacity building and promotes collaborative partnerships between institutes and universities. This agency can be modeled on the European Research Council launched by the European Commission or the Alliance for Accelerating Excellence in Science in Africa launched by the African Union. Having an Asia and the Pacific research council would not only maximize investments but also prevent unnecessary overlaps in R&D funding. National contributions to this council can be adjusted by GDP per capita. Alternatively, the AASSA could expand its mission to take on these new roles.

**Building R&D preparedness** for existing infectious diseases within a reasonable time before an outbreak requires first prioritizing those with the highest epidemic threat for R&D to develop drug and vaccine candidates from fundamental research to Phase II clinical trials.
Individual countries and Asia and the Pacific as a whole should develop and strengthen their national and regional vaccine R&D preparedness. This means strengthening R&D platform technologies that can be used for developing vaccines for different pathogens, including still unknown diseases (Disease X). R&D preparedness requires countries and regions to fund, build, and maintain adequate research infrastructure that is not simply “epidemic specific” but mainly “epidemic sensitive” (Keusch and Lurie 2020). To better target funding for R&D preparedness and avoid overlaps, the status of funded road maps for specific and unknown diseases should be made public. The WHO Global Observatory on Health R&D can monitor the funding for different pathogens, and other organizations such as Policy Research Cures through its G-FINDER survey can also monitor financial flows for R&D, the source of funding, the identity of intermediaries, and the firms that will eventually develop vaccines.

Having in place strong R&D preparedness is essential to support a **rapid and effective R&D response** to develop vaccines and drugs once an outbreak emerges. Stakeholders in vaccine R&D should concomitantly fund a range of vaccine candidates and platforms. Newer platforms do not need to be available in each country and can be shared at a regional location. Vaccine R&D responsiveness during an outbreak demands the rapid sharing of data and the development of technology systems for rapidly identifying antigens and assessing the efficacy and safety of vaccine candidates. Even countries with strong R&D preparedness will have to mobilize new resources to respond to a major infectious disease outbreak. The search for financial resources to fund an R&D response cannot start at the time of the outbreak; such resources should be readily available at short notice. Different financial mechanisms can be explored. The Global Research Collaboration for Infectious Disease Preparedness (GLoPID-R) network can coordinate funding flows into a permanent fund modeled on the Pandemic Emergency Financing Facility that was created and managed by the World Bank to help low-income countries finance their response to epidemics (World Bank 2019). A similar mechanism can be established specifically to finance a rapid R&D response to major infectious disease outbreaks (WHO 2016).
From Lab to Jab: Improving Asia and the Pacific’s Readiness to Produce and Deliver Vaccines

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4

Financing Research and Development for New Vaccines in Developing Countries in Asia and the Pacific

Gavin Yamey, Kaci Kennedy McDade, Wenhui Mao, and Chukwunomso Ekene Osakwe

4.1 Introduction

Many important shifts and innovations have occurred over the past 2 decades in the development of vaccines for neglected and emerging infectious diseases. These include the launch of new public–private product development partnerships (PDPs), the mobilization of funding for vaccine research and development (R&D) from bilateral development agencies and philanthropies, and the emergence of new networks and partnerships devoted to R&D on vaccines for diseases of poverty. In addition, the development of coronavirus disease (COVID-19) vaccines in less than 1 year—the fastest vaccine development in history—has injected optimism that a new vaccine revolution could be underway, using next-generation vaccine platforms such as viral vectors and mRNA (Yamey 2021).

Despite these positive trends, major gaps remain in funding the development of vaccines for emerging infectious diseases and diseases of poverty, especially when it comes to financing late-stage development. The improvements in the landscape have mostly targeted early-stage development. There are many reasons for this funding gap, but three of the most important explanations are (Yamey et al. 2020): First, late-stage trials are costly; there is a financial risk in investing in them and no guarantee of a commercial market, particularly for the most neglected diseases of poverty (patients themselves and low-income country
governments may be unable to pay for vaccines). Second, there is no overarching prioritization, coordination, and governance mechanism for vaccine R&D—the result is that the vaccine R&D landscape remains highly fragmented with multiple overlapping and duplicative efforts. And third, there has been too little inclusion of voices from low- and middle-income countries when it comes to decision-making around vaccine R&D, even though these countries suffer a disproportionate burden of vaccine-preventable illness.

These ongoing funding gaps mean that many emerging and infectious diseases lack safe, high-efficacy vaccines. Many diseases with a high burden in Asia and the Pacific lack licensed, highly effective vaccines. For example, the region has more people living with HIV/AIDS (5.8 million in 2020) than any other region except sub-Saharan Africa (UNAIDS 2021). There are no licensed HIV vaccines yet. Another example is tuberculosis (TB), which is the leading cause of infectious disease deaths in Asia and the Pacific. Over 40% of new annual cases and almost half of all annual TB deaths are in India, Indonesia, and Pakistan alone (OECD 2020a). The only licensed vaccine is the bacille Calmette–Guérin (BCG) vaccine, introduced in 1921. While it provides “moderate protection against severe forms of TB in infants and young children” (Kasaeva 2021), it is ineffective in preventing TB disease in adults, either before or after exposure to TB infection. Finally, hookworm and other soil-transmitted helminths are highly prevalent in Asia and the Pacific. For example, hookworm prevalence is 30% in the Lao People’s Democratic Republic, 29% in Viet Nam, and 28% in Cambodia, while roundworm prevalence is 76% in the Philippines, 72% in Malaysia, and 53% in Myanmar (Silver et al. 2018). Vaccines are needed because the only current way to achieve parasite control is through repeated bouts of mass drug administration.

In addition, neglected infectious diseases affect populations in Asia and the Pacific where the existing vaccines have limitations. For example, over 2 billion people are at high risk of malaria in the region, where the disease is endemic in 17 countries: Papua New Guinea, Solomon Islands, Pakistan, India, Nepal, the Philippines, Indonesia, Myanmar, the Lao People’s Democratic Republic, Cambodia, Thailand, the Democratic People’s Republic of Korea, the People’s Republic of China (PRC), Viet Nam, Bangladesh, the Republic of Korea, and Malaysia (OECD 2020b). There is only one licensed malaria vaccine (RTS,S), and its efficacy against clinical malaria is low: 35.9% efficacy in the first year after vaccination, falling to 2.5% in the fourth year (Olotu et al. 2016).

Around 3.9 billion people worldwide are at risk of dengue, of whom 70% live in Asia and the Pacific, and an estimated 390 million dengue virus infections occur every year, of which 96 million present
clinically (WHO 2022). Only one vaccine has been licensed in selected countries, CYD-TDV (Dengvaxia; Sanofi Pasteur), but often with major restrictions. In their review of dengue vaccine development, Wang and colleagues (2021) note that the vaccine has “demonstrated low efficacy in children and dengue-naïve individuals and also increases the risk of severe dengue in young vaccinated recipients.”

Asia and the Pacific has also been at the epicenter of several emerging infectious diseases, including SARS, avian influenza, and COVID-19, and developing and stockpiling vaccines against emerging threats is a critical foundation of the World Health Organization (WHO) Asia Pacific Strategy for Emerging Diseases (Li and Kasai 2011).

Given this need to develop new vaccines for a range of infectious diseases, there is renewed urgency also to mobilize additional financing for vaccine R&D in Asia and the Pacific. In this chapter, we begin by laying out the estimated financing gap for developing vaccines for neglected and emerging infectious diseases and exploring why this gap persists. We then examine the current landscape of financing for vaccine R&D in the region, focusing on both the strengths and weaknesses. In this landscaping, we describe the main funders and funding recipients, the recent initiatives aimed at raising financing (e.g., public–private partnerships), and the levels of funding that have been mobilized. Next, we look at the value proposition for increased investments in vaccine R&D in the region. Finally, we propose policy options to close the financing gap for vaccine R&D in the region. This analysis was based on a rapid review of the peer-reviewed and gray literature and key informant interviews with relevant experts in Asia and the Pacific. The study was screened and approved for exemption by Duke University’s institutional review board.

### 4.2 Vaccines for Neglected and Emerging Infectious Diseases: The Financing Gap

Understanding how much additional financing is needed for vaccine R&D for neglected and emerging infectious diseases is a crucial first step in closing the financing gap. Unfortunately, for several reasons that will be discussed, very few estimates of this gap exist, and all available estimates are subject to many limitations.

#### 4.2.1 Current Spending on R&D for Neglected Diseases

The best available evidence on current public, private, and philanthropic spending on vaccine R&D for neglected and emerging infectious diseases comes from the annual G-FINDER survey conducted by Policy Cures...
Research, a global health think tank. The survey has been published annually since 2008.¹ The most recent report (Chapman et al. 2022) estimates funding in 2020 for R&D for basic research, drugs, vaccines, biologics, diagnostics, microbicides, vector control products, and “unspecified funding” across 45 disease categories, as well as funding for platform technologies, multi-disease vector control products, core funding for multi-disease R&D organizations, and funding for “unspecified diseases.”

In 2020, total funding was $3.9 billion, a small decrease from the near-record high in 2019. Around a quarter of this total—$1.1 billion—was for vaccine R&D against specific disease categories, $47 million for vaccine delivery technologies and devices, and $24 million for adjuvants and immunomodulators. Table 4.1 shows the breakdown of vaccine R&D funding in 2020 by broad disease category. In section 4.3, we further disaggregate this vaccine R&D funding for neglected diseases to show recipients of funding in Asia and the Pacific and who is funding these recipients.

### Table 4.1: Vaccine R&D Funding for Neglected Diseases by Broad Disease Category, 2020 ($ million)

<table>
<thead>
<tr>
<th>Broad Disease Category</th>
<th>2020 Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV/AIDS</td>
<td>710.31</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>72.94</td>
</tr>
<tr>
<td>Malaria</td>
<td>117.58</td>
</tr>
<tr>
<td>Diarrheal diseases</td>
<td>75.54</td>
</tr>
<tr>
<td>Kinetoplastid diseases</td>
<td>4.66</td>
</tr>
<tr>
<td>Helminth infections (worms and flukes)</td>
<td>5.52</td>
</tr>
<tr>
<td>Salmonella infections</td>
<td>32.91</td>
</tr>
<tr>
<td>Bacterial pneumonia and meningitis</td>
<td>61.06</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>2.46</td>
</tr>
<tr>
<td>Rheumatic fever</td>
<td>15.59</td>
</tr>
<tr>
<td>Leprosy</td>
<td>0.43</td>
</tr>
<tr>
<td>Buruli ulcer</td>
<td>0.02</td>
</tr>
<tr>
<td>Trachoma</td>
<td>1.91</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,100.93</strong></td>
</tr>
</tbody>
</table>

R&D = research and development.

Source: Chapman et al. (2022).

¹ The survey reports are archived on the Policy Cures Research website at https://www.policycuresresearch.org/analysis/.
Policy Cures Research recently published their estimates of annual funding for such emerging infectious diseases from 2014 to 2018, which showed that funding reached a record high of $886 million in 2018 (Chapman et al. 2020). The sharp rise in annual funding for R&D for such diseases was driven by the Ebola and Zika epidemics, the launch of the Coalition for Epidemic Preparedness Innovations (CEPI), and the rising interest in funding R&D for what the R&D Blueprint for Action to Prevent Epidemics (WHO 2016) calls “Disease X” (i.e., an epidemic or pandemic caused by a pathogen currently unknown to cause human disease).

Out of the $886 million spent in 2018, about 40% ($350 million) was invested in vaccines for specific emerging infectious diseases. The breakdown of vaccine R&D financing into broad disease categories is shown in Table 4.2. In addition, for Disease X and other R&D, $10.09 million was spent on adjuvants and immunomodulators, $2.57 million on vaccine delivery technologies and devices, and $7.78 million on vaccine platforms and multi-family vaccines. In section 4.3, we further disaggregate this vaccine R&D funding for emerging infectious diseases by funder type.

<table>
<thead>
<tr>
<th>Broad Disease Category</th>
<th>2018 Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filoviruses: Ebola and Marburg</td>
<td>187.63</td>
</tr>
<tr>
<td>Zika virus</td>
<td>102.59</td>
</tr>
<tr>
<td>Arenaviruses: Lassa</td>
<td>25.16</td>
</tr>
<tr>
<td>Coronaviruses: MERS and SARS</td>
<td>22.14</td>
</tr>
<tr>
<td>Bunyaviruses: CCHF and RVF</td>
<td>10.4</td>
</tr>
<tr>
<td>Henipaviruses: Nipah and others</td>
<td>2.39</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>350.31</strong></td>
</tr>
</tbody>
</table>

CCHF = Crimean–Congo hemorrhagic fever, MERS = Middle East respiratory syndrome, R&D = research and development, RVF = Rift Valley fever, SARS = severe acute respiratory syndrome.

Source: Chapman et al. (2020).

### 4.2.2 Estimates of R&D Funding Needs

In the previous section, we summarized the estimates of the current levels of financing of vaccine R&D for neglected and emerging infectious diseases. How do these levels compare with estimates of funding needs—in other words, what is the likely financing gap?
There is no straightforward answer to this question, given the challenges in estimating the costs to develop vaccines for neglected and emerging infectious diseases. Proprietary concerns, for example, have meant that vaccine companies are reluctant to share information on the cost, success rate, and cycle time per phase for vaccine development. The different cost structures for developing vaccines for different infections are poorly understood, as are the differences between costs for simple versus complex vaccines.

Despite these limitations, several recent efforts have attempted to estimate vaccine R&D costs for neglected and emerging infectious diseases, which provide a helpful starting point in understanding the likely size of the financing gap. We acknowledge that these are necessarily crude numbers, but no accurate figures on the gap are available.

A. The Cost to Develop Vaccines for Neglected Diseases

In 2018, in the first study of its kind, Young and colleagues (2020) conducted a product pipeline portfolio review for 35 neglected diseases and then used a new financial modeling tool, the Portfolio to Impact (P2I) tool, to estimate the costs to move these existing product candidates through the pipeline over the next decade and the likely launches. Given that the existing pipeline was unlikely to yield several highly needed technologies, the authors also estimated the costs to develop a set of 18 priority “missing” products. These priority products were highly effective vaccines for HIV, TB, malaria, hepatitis C, diarrhea (a combined vaccine against rotavirus, enterotoxigenic Escherichia coli, typhoid, and shigella), a new TB drug co-formulation, and a new drug for each of 12 different neglected tropical diseases. The study included costs for advanced preclinical to Phase III trials (i.e., it did not estimate earlier basic research or any costs after Phase III, so it underestimated total costs).

They found that 538 product candidates were in the pipeline, as of 31 August 2017. They estimated that about $16.3 billion would be needed to move these candidates through the pipeline, with three-quarters of the costs incurred in the first 5 years, resulting in about 128 expected product launches. Based on the existing pipeline, they found that “there would be few launches of complex new chemical entities; launches of highly efficacious HIV, tuberculosis, or malaria vaccines would be unlikely.” Launching each of the 18 key missing products would cost an additional $13.6 billion, assuming the lowest product complexity, or $21.8 billion, assuming the highest complexity. During 2017–2022, total estimated costs to move existing candidates through the pipeline and develop these 18 missing products would be $4.5 billion per year (low-complexity missing products) or $5.8 billion (high-complexity missing products). Since annual global spending on
neglected disease R&D was about $3 billion from 2008 to 2017, the study suggested that the **annual funding gap over the next 5 years was at least $1.5 billion to $2.8 billion**. Focusing on vaccine development alone, they estimated that $9 billion would be needed to move vaccine candidates through the pipeline (again, three-quarters of the costs would be incurred in the first 5 years). Launching “missing” vaccines for HIV, TB, malaria, hepatitis C, and diarrheal diseases would cost an additional $12.55 billion to $13.2 billion (depending on vaccine complexity). Thus, total estimated costs during 2017–2022 to move existing vaccine candidates through the pipeline and develop these five missing vaccines would be $16.1 billion to $16.7 billion, or **$3.2 billion to $3.3 billion annually**.

As shown in Table 4.1, annual spending on vaccine R&D for HIV, TB, malaria, hepatitis C, and diarrheal diseases was about $1 billion in 2020. Thus, we estimate that the funding gap for these five neglected diseases alone is **$2 billion annually**.

### B. The Cost to Develop Vaccines for Emerging Infectious Diseases

Gouglas and colleagues (2018) conducted a pipeline portfolio review of vaccine candidates for 11 diseases with epidemic potential and used a stochastic optimization model to estimate the minimum costs to progress at least one vaccine for each disease through to the end of Phase IIa. The 11 diseases included in the study were the R&D Blueprint diseases at the time: Crimean–Congo hemorrhagic fever (CCHF), chikungunya, Ebola, Lassa, Marburg, Middle East respiratory syndrome coronavirus (MERS), Nipah, Rift Valley fever, severe acute respiratory syndrome (SARS), severe fever with thrombocytopenia syndrome (SFTS), and Zika.

Given the likely success rates at each phase of development, Gouglas and colleagues estimated that the average cost of advancing at least one vaccine from preclinical through to the end of Phase IIa ranges from $319 million to $469 million, which includes the cumulative cost of failed vaccine candidates through the R&D process. They conclude that “assuming these candidates and funding were made available, progressing at least one vaccine through to the end of phase 2a for each of the 11 epidemic infectious diseases would cost a minimum of $2.8 billion–$3.7 billion.”

The authors estimate that the average timeline bringing emerging infectious disease vaccine development projects from preclinical through to the end of Phase II is 6–7 years. Thus, the annualized financing need is about $400 million–$520 million. Table 4.3 shows that annual spending on the R&D Blueprint diseases was $350 million in 2018, suggesting an annual funding gap of **$50 million–$170 million**.
4.3 Barriers to Funding Vaccine R&D

In section 4.2, we showed that the annual financing gap for vaccine R&D for neglected diseases is about $2 billion and the gap for vaccine R&D for emerging infectious diseases is about $50 million–$70 million. Why does such a gap persist? In other words, what have been the barriers to research funders mobilizing additional financing? As described, there certainly has been increased attention from funders toward R&D for neglected and emerging infectious diseases, but the underlying reasons for the ongoing gap have not been addressed in a fundamental, game-changing way. In this section, we briefly describe five of the most important barriers to mobilizing finance.

4.3.1 Market Failure

Market failure continues to impede vaccine R&D financing, especially for the “most neglected” diseases (those that currently attract the lowest amounts of funding). The patients in countries most affected by these diseases, including those in Asia and the Pacific—as well as the governments of these countries—do not have much purchasing power. Such purchasing power is particularly limited in low-income countries (LICs) and lower middle-income countries (LMICs), such as Cambodia, the Democratic People’s Republic of Korea, Solomon Islands, Timor-Leste, and Viet Nam. Pharmaceutical companies see little financial incentive in making vaccines for diseases that disproportionately affect LICs and LMICs—they do not have enough of a market for such vaccines in high-income countries (HICs).

One way to attract industry to develop vaccines for neglected and emerging infectious diseases is through public–private product development partnerships (PDPs), which we describe in section 4.4. However, it has been hard to persuade industry to enter into PDPs for the most neglected diseases (Yamey 2002). As we have previously argued, when industry sees at least some market (e.g., HIV affects people in rich nations), then the public sector can use bargaining power (i.e., push and pull mechanisms) to persuade industry to enter into PDPs, as it did with the International AIDS Vaccine Initiative. Such mechanisms include reducing the costs of R&D through grants, tax credits, or public support for clinical trials or creating an advance purchase commitment that guarantees purchase of vaccines that come to market. However, when it comes to the world’s most neglected diseases, “these present absolutely no market opportunities. Without such opportunities, there is no incentive for the pharmaceutical industry to invest in drug research.
and development. The patients have no purchasing power, no vocal advocacy group is pleading for their needs, and no strategic interests—military or security—are driving concern about these conditions. This is why no public–private partnerships exist specifically for the most neglected diseases” (Yamey 2002).

Without a market, vaccine companies are particularly reluctant to invest in late-stage vaccine trials, as these are the costliest development phase. Rappuoli, Black, and Bloom (2019) found that late-stage trials are responsible for about 70% of all neglected disease vaccine development costs, whereas discovery is an estimated 10% and early development 20% of the R&D budget.

4.3.2 The Free-Rider Problem

A second barrier to closing the vaccine finance R&D gap is the so-called “free rider” problem. As Moon, Bermudez, and ’t Hoen (2019) state, “If one country can benefit from the investment of another, there is a powerful temptation to ‘free-ride’ on the other’s efforts; the end result may be aggregate global underinvestment in R&D.” This type of market failure means some countries may stay on the sidelines when it comes to funding R&D—they can “reap the benefits without taking any risks” (Yamey et al. 2020).

When it comes to vaccine development for neglected and emerging infectious diseases, the free-rider problem has been well described. For example, Kremer and Snyder (2020) estimated the magnitude of the free-rider problem as it relates to developing vaccines for endemic neglected diseases such as HIV and malaria. More specifically, they estimated the government subsidy per vaccine that would be needed to overcome this problem. For their analysis, they assume a basic reproductive number ($R_0$) of 4. They find that “the free-rider problem exacerbates monopoly incentives to distort quantity downward to keep prices high. We find that to counteract the severe distortions and achieve the first best when $R_0 = 4$ would require a per-dose subsidy for the vaccine that would be roughly three times estimates of the monetary value that those afflicted with the disease would be prepared to pay to recover. A more practical government policy would therefore involve negotiating a bulk purchase for the population.”
4.3.3 Poor Coordination of the Global Vaccine R&D Enterprise for Neglected and Emerging Infectious Diseases

The past 2 decades have seen the emergence of new mechanisms and initiatives aimed at mobilizing financing for neglected and emerging infectious disease vaccine R&D, including in Asia and the Pacific. Examples include the International AIDS Vaccine Initiative, CEPI, the United States Biomedical Advanced Research and Development Authority, the Meningitis Vaccine Project, and the Japan-based Global Health Innovative Technology Fund or Global Health Innovative Technology Fund. However, one major governance problem is that no clear, consistent global mechanism for R&D prioritization and coordination exists. There are several overlapping initiatives. The landscape of vaccine R&D financing suffers from duplication, fragmentation, and inefficiencies, all of which can lead to wasted resources and delays in vaccine development.

This problem is long-standing. For example, in 2012, the WHO Consultative Expert Working Group on Research and Development: Financing and Coordination concluded that the absence of action to close the global health R&D financing gap “is itself a reflection of the difficulty of improving coordination precisely because the field is so fragmented and the interests of funders and researchers are so diverse” (WHO 2012). In their analysis called “In search of global governance for research in epidemics,” Peters and colleagues (2017) argued that Ebola vaccine development during the 2014–2016 epidemic in Western Africa was hindered by poor overarching vaccine R&D governance.

While WHO has recognized and begun to address this problem—such as through the launch of its Global Observatory on Health R&D and its Target Product Profile Directory (Moorthy and Yamey 2022)—these efforts remain at a nascent stage.

4.3.4 Exclusion of Policymakers from Low-Income and Lower Middle-Income Countries in Funding Decisions

A fourth barrier to raising additional financing for vaccine R&D for neglected and emerging infectious diseases is that key decision-making processes and forums have done poorly at including decision-makers

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from countries that are the most affected by these diseases. Decision-making on funding for such vaccines, especially in PDPs, has tended to be “top down” rather than “bottom up”—in other words, policymakers from LICs and lower MICs, who are tackling the highest burden of these diseases, are often not at the decision-making table. The result is that they are left out “when it comes to deciding on what gets funded, where research is conducted, who gets access to intellectual property, and where and how the technologies end up being manufactured” (Yamey et al. 2020).

### 4.3.5 Limited Vaccine Manufacturing Capacity in High-Burden Countries

Finally, when it comes to what Rappuoli, Black, and Bloom (2019) call the “Valley of Death in the late vaccine development phase”—the lack of financing for Phase III trials—many LICs and LMICs are stuck in a catch-22. Because they may lack clinical trial capacity and expertise—for example, weak regulatory processes for clinical trials of vaccines, too few facilities to conduct trials, and lack of trained personnel—funders may be reluctant to invest in R&D in these settings. Improving capacity and expertise would help to create a virtuous circle that could attract new financing.

In LICs and LMICs in Asia and the Pacific, the existing vaccine manufacturing capacity (described in section 4.4) is mostly traditional (e.g., manufacturing cell culture-based inactivated vaccines) and small scale. Vaccine manufacturers in the region have not yet adopted the innovative, next-generation vaccine R&D platforms that were validated during the COVID-19 pandemic such as mRNA and viral vectors (Yamey 2021).

### 4.4 The Landscape of Vaccine R&D Financing in Asia and the Pacific

Earlier in this chapter, we showed that about $1.1 billion is invested annually in developing vaccines for neglected diseases and about $350 million annually in developing vaccines for the R&D Blueprint diseases. We also estimated that the annual financing gap for vaccine R&D for neglected diseases is $2 billion and the gap for vaccine R&D for emerging infectious diseases $50 million–$70 million. We examined why this financing gap persists, including market failure, the free-rider problem, poor governance and coordination of the global vaccine R&D enterprise, exclusion of decision-makers from LICs and LMICs
in decisions about vaccine R&D, and limited vaccine manufacturing capacity in many of these countries. We now focus on the vaccine R&D financing landscape in the region itself to identify weaknesses and opportunities for future resource mobilization.

### 4.4.1 Levels of Financing for Vaccine R&D

We conducted a rapid search of the G-FINDER database to estimate how much funding there is for developing vaccines in Asia and the Pacific. In the following paragraphs, we summarize our initial findings on total funding for the financial years 2018, 2019, and 2020 and also give an annualized estimate across this 3-year period. The G-FINDER database does not capture all vaccine R&D funders (e.g., it does not capture smaller funders in Thailand), so our numbers are likely to underestimate total funding.

#### A. Funding for Vaccine R&D for Neglected Diseases

We estimate that $105.1 million was invested in vaccine R&D for neglected diseases in Asia and the Pacific during 2018–2020, or an average of $35 million annually. Table 4.3 shows the breakdown of this total by funder and recipient type (academic, national government, PDP, or other). The largest amount of funding over this 3-year period was from the United States (US) ($48.9 million), followed by Australia ($26.3 million) and then industry ($14.7 million). Around two-thirds of all funding went to academic and research institutions and a quarter to PDPs. Out of the total of $105.1 million during the same period, only $37.2 million was funding that came from within the region.

Table 4.4 shows that the largest financing sources from within the region during 2018–2020 were Australia's Medical Research Future Fund ($17.6 million), Australia’s National Health and Medical Research Council ($8.2 million), and the Indian Council on Medical Research ($5.2 million). Table 4.5 shows the breakdown of the $105.1 million by disease area: the largest amount is for bacterial pneumonia and meningitis ($33.0 million), followed by rheumatic fever ($25.3 million), salmonella infections ($22.0 million), and diarrheal diseases ($11.8 million).

Thus, the overall level of funding—about $35 million per year—is tiny compared with the estimated funding gap of $2 billion per year, and there are very low levels of funding for diseases that have a high burden in Asia and the Pacific.
## Table 4.3: Sources of Funding for Neglected Disease Vaccine R&D in Asia and the Pacific, 2018–2020 ($)

<table>
<thead>
<tr>
<th>Funder</th>
<th>Country Income Status</th>
<th>Funding to Academic and Research Institutions</th>
<th>Funding to National Government Agencies</th>
<th>Funding to Product Development Partnerships</th>
<th>Funding to Other Recipients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>HIC</td>
<td>20,922,895</td>
<td>4,447,139</td>
<td>23,523,015</td>
<td></td>
<td>48,893,049</td>
</tr>
<tr>
<td>Australia</td>
<td>HIC</td>
<td>26,254,622</td>
<td></td>
<td></td>
<td></td>
<td>26,254,622</td>
</tr>
<tr>
<td>Industry</td>
<td></td>
<td>14,620,304</td>
<td></td>
<td></td>
<td></td>
<td>14,730,069</td>
</tr>
<tr>
<td>India</td>
<td>LMIC</td>
<td>3,407,105</td>
<td>6,049,071</td>
<td></td>
<td></td>
<td>9,589,156</td>
</tr>
<tr>
<td>Switzerland</td>
<td>HIC</td>
<td>2,047,242</td>
<td></td>
<td></td>
<td></td>
<td>2,047,242</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>HIC</td>
<td>144,557</td>
<td>460,262</td>
<td>1,078,761</td>
<td></td>
<td>1,683,581</td>
</tr>
<tr>
<td>Republic of Korea</td>
<td>HIC</td>
<td></td>
<td></td>
<td></td>
<td>649,651</td>
<td>649,651</td>
</tr>
<tr>
<td>European Union</td>
<td>HIC</td>
<td>57,772</td>
<td></td>
<td>472,648</td>
<td></td>
<td>530,420</td>
</tr>
<tr>
<td>New Zealand</td>
<td>HIC</td>
<td>469,466</td>
<td></td>
<td></td>
<td></td>
<td>469,466</td>
</tr>
<tr>
<td>Japan</td>
<td>HIC</td>
<td>170,430</td>
<td>91,343</td>
<td></td>
<td></td>
<td>261,772</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>68,094,392</td>
<td>11,047,815</td>
<td>25,833,840</td>
<td>132,980</td>
<td>105,109,027</td>
</tr>
</tbody>
</table>

HIC = high-income country, LMIC = lower middle-income country, R&D = research and development.

Source: Authors’ analysis.

## Table 4.4: Sources of Funding for Neglected Disease Vaccine R&D in Asia and the Pacific from Funders Based in the Region, 2018–2020 ($)

<table>
<thead>
<tr>
<th>Funder</th>
<th>Country Income Status</th>
<th>Amount of Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>HIC</td>
<td>26,254,622</td>
</tr>
<tr>
<td>MRFF</td>
<td></td>
<td>17,646,874</td>
</tr>
<tr>
<td>NHMRC</td>
<td></td>
<td>8,210,864</td>
</tr>
<tr>
<td>Australian Centre for HIV and Hepatitis Virology</td>
<td></td>
<td>305,047</td>
</tr>
<tr>
<td>Melbourne Children’s</td>
<td></td>
<td>48,407</td>
</tr>
<tr>
<td>CASS Foundation</td>
<td></td>
<td>39,960</td>
</tr>
<tr>
<td>Far North Queensland Hospital Foundation</td>
<td></td>
<td>3,470</td>
</tr>
</tbody>
</table>

continued on next page
Table 4.4 continued

<table>
<thead>
<tr>
<th>Funder</th>
<th>Country Income Status</th>
<th>Amount of Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>LMIC</td>
<td>9,589,156</td>
</tr>
<tr>
<td>ICMR</td>
<td></td>
<td>5,249,732</td>
</tr>
<tr>
<td>Undisclosed</td>
<td></td>
<td>2,643,455</td>
</tr>
<tr>
<td>Indian DBT</td>
<td></td>
<td>1,695,969</td>
</tr>
<tr>
<td>Republic of Korea</td>
<td>HIC</td>
<td>649,651</td>
</tr>
<tr>
<td>Ministry of Food and Drug Safety</td>
<td></td>
<td>647,844</td>
</tr>
<tr>
<td>Kim &amp; Chang</td>
<td></td>
<td>1,807</td>
</tr>
<tr>
<td>New Zealand</td>
<td>HIC</td>
<td>469,466</td>
</tr>
<tr>
<td>Health Research Council of New Zealand</td>
<td></td>
<td>469,466</td>
</tr>
<tr>
<td>Japan</td>
<td>HIC</td>
<td>261,772</td>
</tr>
<tr>
<td>Japan Society for the Promotion of Science</td>
<td></td>
<td>261,772</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>37,224,667</td>
</tr>
</tbody>
</table>

CASS = Contributing to Australian Scholarship and Science, DBT = Department of Biotechnology, HIC = high-income country, ICMR = Indian Council of Medical Research, LMIC = lower middle-income country, MRFF = Medical Research Future Fund, NHRMC = National Health and Medical Research Council, R&D = research and development.

Source: Authors’ analysis.

Table 4.5: Funding for Neglected Disease Vaccine R&D in Asia and the Pacific by Disease, 2018-2020 ($) 

<table>
<thead>
<tr>
<th>Disease</th>
<th>Amount of Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial pneumonia and meningitis</td>
<td>32,982,035</td>
</tr>
<tr>
<td>Rheumatic fever</td>
<td>25,326,794</td>
</tr>
<tr>
<td>Salmonella infections</td>
<td>22,050,095</td>
</tr>
<tr>
<td>Diarrheal diseases</td>
<td>11,795,667</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>5,594,660</td>
</tr>
<tr>
<td>Malaria</td>
<td>2,250,078</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>2,212,473</td>
</tr>
<tr>
<td>Kinetoplastid diseases</td>
<td>1,096,246</td>
</tr>
<tr>
<td>Helminth infections (worms and flukes)</td>
<td>880,399</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>859,938</td>
</tr>
<tr>
<td>Leprosy</td>
<td>37,478</td>
</tr>
<tr>
<td>Buruli ulcer</td>
<td>23,165</td>
</tr>
<tr>
<td>Total</td>
<td>105,109,027</td>
</tr>
</tbody>
</table>

R&D = research and development.

Source: Authors’ analysis.
B. Funding for Vaccine R&D for Emerging Infectious Diseases

We estimate that $11.3 million was invested in vaccine R&D for emerging infectious diseases in Asia and the Pacific during 2018–2020, or an average of $3.8 million annually (a low level of funding compared with the $50 million–$70 million annual funding gap for these diseases). Table 4.6 shows the breakdown of this total by funder and recipient type (academic, national government, or PDP). The Republic of Korea is by far the largest funder ($7.8 million over the 3-year period), and all of its funding is to PDPs. Table 4.7 shows the breakdown of funding by disease. Almost two-thirds of all funding was for coronaviral diseases (including MERS, SARS, and COVID-19).

Table 4.6: Sources of Funding for Emerging Infectious Disease Vaccine R&D in Asia and the Pacific, 2018–2020

<table>
<thead>
<tr>
<th>Funder</th>
<th>Income Status</th>
<th>Funding to Academic and Research Institutions ($)</th>
<th>Funding to National Government Agencies ($)</th>
<th>Funding to Product Development Partnerships ($)</th>
<th>Total ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Republic of Korea</td>
<td>HIC</td>
<td>7,793,253</td>
<td></td>
<td></td>
<td>7,793,253</td>
</tr>
<tr>
<td>Gyeongbuk Institute for Bio Industry</td>
<td></td>
<td>163,666</td>
<td></td>
<td></td>
<td>163,666</td>
</tr>
<tr>
<td>KDCA</td>
<td></td>
<td>327,392</td>
<td></td>
<td></td>
<td>327,392</td>
</tr>
<tr>
<td>KHIDI</td>
<td></td>
<td>802,218</td>
<td></td>
<td></td>
<td>802,218</td>
</tr>
<tr>
<td>Samkwang Medical Laboratories</td>
<td></td>
<td>170,377</td>
<td></td>
<td></td>
<td>170,377</td>
</tr>
<tr>
<td>Samsung Foundation</td>
<td></td>
<td>6,329,600</td>
<td></td>
<td></td>
<td>6,329,600</td>
</tr>
<tr>
<td>Australia</td>
<td>HIC</td>
<td>1,665,900</td>
<td></td>
<td></td>
<td>1,665,900</td>
</tr>
<tr>
<td>NHMRC</td>
<td></td>
<td>1,665,900</td>
<td></td>
<td></td>
<td>1,665,900</td>
</tr>
<tr>
<td>India</td>
<td>LMIC</td>
<td>722,131</td>
<td>795,921</td>
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<td>1,518,052</td>
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<tr>
<td>Indian DBT</td>
<td></td>
<td>175,122</td>
<td></td>
<td></td>
<td>175,122</td>
</tr>
<tr>
<td>Department of Science and Technology</td>
<td></td>
<td>40,933</td>
<td></td>
<td></td>
<td>40,933</td>
</tr>
<tr>
<td>ICMR</td>
<td></td>
<td>752,031</td>
<td></td>
<td></td>
<td>752,031</td>
</tr>
<tr>
<td>Undisclosed</td>
<td></td>
<td>547,009</td>
<td>2,957</td>
<td></td>
<td>549,966</td>
</tr>
<tr>
<td>Industry</td>
<td></td>
<td>138,365</td>
<td></td>
<td></td>
<td>138,365</td>
</tr>
<tr>
<td>Japan</td>
<td>HIC</td>
<td>56,046</td>
<td>41,376</td>
<td></td>
<td>97,422</td>
</tr>
<tr>
<td>Japan Society for the Promotion of Science</td>
<td></td>
<td>56,046</td>
<td>41,376</td>
<td></td>
<td>97,422</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>2,582,442</td>
<td>837,279</td>
<td>7,793,253</td>
<td>11,212,992</td>
</tr>
</tbody>
</table>

DBT = Department of Biotechnology, HIC = high-income country, ICMR = Indian Council of Medical Research, KDCA = Korea Disease Control and Prevention Agency, KHIDI = Korea Health Industry Development Institute, LMIC = lower middle-income country, NHMRC = National Health and Medical Research Council, R&D = research and development.

Source: Authors’ analysis.
4.4.2 Current Sources of Financing for Vaccine R&D

The three key sources of financing for vaccine R&D in Asia and the Pacific are public, private, and philanthropic (Figure 4.1).

A. Public Funding for Vaccine R&D
Public funding is chiefly from national research agencies and national aid or development agencies—both within and outside the region (see Tables 4.3, 4.4, and 4.6). Many national governments in Asia and the Pacific fund universities and research institutes to conduct vaccine R&D. These efforts are mostly small scale, with some exceptions such as those of Australia’s Medical Research Future Fund and National Health and Medical Research Council and of the Indian Council of Medical Research (Tables 4.4 and 4.6).

Little public information is available on the PRC government’s funding of vaccine R&D, but its investments in COVID-19 vaccine development, including launching the world’s first COVID-19 vaccine trial in Wuhan (Zhu et al. 2020), have helped to shine a light on its R&D of other vaccines. Hu and Chen (2021) note that the PRC’s COVID-19 vaccine R&D represents the success of state-driven collaborative research, but such an approach has not been strategically applied to other vaccines. The authors say that “compared with developed countries such as the US and the UK, China generally lags behind in non-COVID-19 vaccine R&D, production and regulatory capacity.”

Table 4.7: Funding for Emerging Infectious Disease Vaccine R&D in Asia and the Pacific by Disease, 2018–2020 ($)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Amount of Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronaviral diseases (including MERS, SARS, COVID-19)</td>
<td>7,283,572</td>
</tr>
<tr>
<td>Zika</td>
<td>1,606,167</td>
</tr>
<tr>
<td>Chikungunya</td>
<td>1,368,780</td>
</tr>
<tr>
<td>Filoviral diseases (including Ebola, Marburg)</td>
<td>536,397</td>
</tr>
<tr>
<td>Bunyaviral diseases (including CCHF, RVF, SFTS)</td>
<td>418,075</td>
</tr>
<tr>
<td>Total</td>
<td>11,212,992</td>
</tr>
</tbody>
</table>

CCHF = Crimean–Congo hemorrhagic fever, COVID-19 = coronavirus disease, MERS = Middle East respiratory syndrome, R&D = research and development, RVF = Rift Valley fever, SARS = severe acute respiratory syndrome, SFTS = severe fever with thrombocytopenia syndrome.

Source: Authors’ analysis.
Key informants interviewed for this analysis argued that government-funded academic research on vaccines in Asia and the Pacific is not yet at a level that is ready for industry translation. There has been little in the way of adopting and adapting newer vaccine technologies and platforms or improving vaccine R&D infrastructure, and R&D has been traditional (e.g., developing inactivated vaccines via cell culture), as mentioned earlier. Few countries in the region have made any public commitments to stepping up funding for vaccine R&D to develop vaccines that the region needs (e.g., vaccines for dengue, Japanese encephalitis, and malaria). One exception is the Republic of Korea—the government announced in January 2021 that “it would spend KRW41.9 billion (US$37 million) to develop treatments and vaccines against new infections as part of a KRW5.8 trillion (US$5.2 billion) science and ICT budget for this year – a 12% rise on 2020 with a focus on basic research, as well as new technologies such as artificial intelligence to drive its innovation-led economy” (Sharma 2021).

B. Private Funding for Vaccine R&D
Private financing comes from domestic industry, multinational companies, and foreign direct investment. However, the amount of funding is small. During 2018–2020, the Policy Cures Research database captures only $14.7 million in industry funding for neglected disease vaccine R&D, though it is possible that proprietary concerns impede reporting.

C. Philanthropic Funding for Vaccine R&D
There has been some philanthropic support for vaccine R&D in Asia and the Pacific—for example, the Bill & Melinda Gates Foundation (2021) has funded human papillomavirus or HPV vaccine R&D at the Serum Institute of India, as well as measles and rubella vaccine development at PT Bio Farma (Persero) in Indonesia (Bill & Melinda Gates Foundation 2018). The Jack Ma Foundation funded a COVID-19 research and prevention fund, and the Alibaba Foundation donated CNY100 million for COVID-19-related research.

Key informants noted that two Asian philanthropies—the Tahir Foundation and the Li Ka Shing Foundation—have funded health research initiatives in Asia and the Pacific (e.g., dengue control and laboratory upgrades) and so could be a source of future funding for vaccine R&D. Several initiatives, described later, also aggregate private funding with public and philanthropic funding through PDPs.
4.4.3 Innovations in Financing Vaccine R&D

In addition to direct government, private, and philanthropic funding of vaccine R&D, innovations in the governance of vaccine R&D financing have led to additional resource mobilization. These innovations have included PDPs and regional approaches to financing.

A. Product Development Partnerships

PDPs have become an important vehicle for vaccine R&D financing. During 2018–2020, PDPs were responsible for about a quarter of the neglected disease vaccine R&D financing in Asia and the Pacific. For example, the PDP PATH supported a Japanese encephalitis vaccine developed by the Chengdu Institute of Biological Products Co., Ltd. in the PRC to achieve WHO prequalification (PATH 2013). A partnership between PATH, WHO, the governments of Viet Nam and the US, and the Institute of Vaccines and Medical Biologicals in Viet Nam led to the development and licensure of a seasonal influenza vaccine produced in Viet Nam (PATH 2019). Finally, the Republic of Korea’s International Vaccine Institute is a nonprofit PDP that develops vaccines for global health. It has 160 partners from government (with core funding from the governments of the Republic of Korea, Sweden, India, and Finland), industry, philanthropy (e.g., grants from the Bill & Melinda Gates Foundation, the Wellcome Trust, and the Samsung Life Public
Welfare Foundation), academia, and multilateral and international organizations (e.g., Gavi, the Vaccine Alliance; United Nations Children’s Fund; CEPI; and WHO). The International Vaccine Institute supports technology transfer and provides technical and financial support for process development and scale-up to clinical development, registration, and WHO prequalification. Its portfolio includes cholera, typhoid, dengue, MERS, schistosomiasis, chikungunya, COVID-19, HPV, TB, and antimicrobial resistance.

Japan’s Global Health Innovative Technology Fund is a PDP that has invested $276 million to date for drug, diagnostic, and vaccine R&D in Japan for malaria, TB, and neglected tropical diseases. About a quarter (24%) of investments have been for vaccine R&D. Most of the total funding (57%) has been for preclinical research, 26% for clinical research, and 17% for discovery. The Republic of Korea’s Research Investment for Global Health Technology (RIGHT) Foundation, launched in July 2018, is a partnership between the Korean government, Korean life science companies, and international funders such as the Bill & Melinda Gates Foundation. The RIGHT Foundation finances the development of drugs, diagnostics, and vaccines for a range of neglected diseases, including soil-transmitted helminth infections, malaria, and TB. By September 2020, it had mobilized over W50 billion ($44 million), half from the government, and a quarter each from Korean companies and the Bill & Melinda Gates Foundation (Hotez et al. 2020). The RIGHT Foundation has invested in the development of two vaccines—one for cholera and a hexavalent vaccine (diphtheria whole-cell pertussis-tetanus toxoid vaccine, inactivated polio vaccine, recombinant hepatitis B vaccine, and Haemophilus influenzae type b or Hib vaccine).

B. Regional Approaches
Regional approaches to fostering vaccine R&D in Asia and the Pacific have mostly focused on enhancing research collaboration, such as through the Association of Academies and Societies of Sciences in Asia. A more recent regional initiative, the Asia and the Pacific Vaccine Access Facility (APVAX), has focused on COVID-19 vaccine procurement. APVAX has a $9 billion budget from the Asian Development Bank, which it has used for both grants and loans (Asian Development Bank 2020). While APVAX is not directly financing vaccine R&D, the pooled purchasing efforts by large-scale regional procurement mechanisms such as APVAX and the African Vaccine Acquisition Trust, launched by the African Union, help provide a guaranteed market for new vaccines, thus supporting R&D.
4.5 Mobilizing Additional Vaccine R&D Financing: The Value Proposition

We have argued that there is currently underinvestment in vaccine R&D financing in Asia and the Pacific. Why should investment be increased? In this section, we briefly lay out the value proposition for increasing the levels of investment in vaccine R&D in the region. We focus on the costs of inaction and the large economic returns to such investments.

4.5.1 The High Costs of Inaction

Developing new effective vaccines could prevent a lot of suffering, disability, and death— as well as economic harm—from neglected and emerging infectious diseases. COVID-19 has shown the scale of health, social, and economic devastation that an emerging infectious disease can cause. For example, the International Monetary Fund estimates that the economic losses COVID-19 has caused will be $13.8 trillion from 2020 to 2024 (Gopinath 2022). Estimated annual losses from influenza pandemic risk are about $500 billion or 0.6% of global income per year (Fan, Jamison, and Summers 2018). Developing new vaccines is also an important strategy for preventing antimicrobial resistance, which in 40 years could lead to an annual gross domestic product loss of about $454 billion per year if current rates of antimicrobial resistance persist (Naylor et al. 2018). The levels of funding needed to develop vaccines for neglected and emerging infectious diseases are tiny compared to the scale of the economic losses these diseases cause.

4.5.2 The Enormous Health and Economic Returns to Investment

In addition to averting a huge number of deaths and disability-adjusted life years (DALYs), investing in vaccines can reap large economic returns, especially through regional investment hubs. For example, in the first study of its kind, Schäferhoff and colleagues (2022) applied investment case modeling and assessed how many cases, deaths, and DALYs the development and manufacturing of new technologies (therapeutics and vaccines) could avert in three middle-income countries (MICs): India, Kenya, and South Africa. They then estimated the economic benefits that might accrue from making these investments and
developed benefit–cost ratios (BCRs) for each of the three countries. The study modeled development of new therapeutics and vaccines for five infectious diseases: HIV, TB, malaria, pneumonia, and diarrheal diseases. The authors found that scaling up such investments in India from 2021 to 2036, provided that the technologies were for a regional market (all of Southeast Asia), could avert almost 9.8 million deaths and 374.4 million DALYs in Southeast Asia. The regional economic returns would outweigh investments by a factor of 68 (i.e., a BCR of 68:1).

Previous vaccine development has also had large economic returns. The polio vaccine was developed through a $26 million investment by the March of Dimes. In the US alone, since routine vaccination was introduced, over 160,000 poliomyelitis deaths and about 1.1 million cases of paralytic polio had been prevented by 2006. Treatment cost savings had generated a net benefit of around $180 billion (Thompson and Tebbens 2006).

4.6 Policy Options to Increase Vaccine R&D Financing in Asia and the Pacific

In section 4.2, we showed that the annual financing gap for vaccine R&D for neglected diseases is about $2 billion and the gap for vaccine R&D for emerging infectious diseases is about $50 million–$70 million. In section 4.3, we examined the reasons for this ongoing financing gap. In section 4.4, we estimated that in Asia and the Pacific from 2018 to 2020, only about $35 million annually was being invested in neglected disease vaccine R&D and $3.8 million annually in emerging infectious disease vaccine R&D—very low levels of financing compared with the need. Nevertheless, many developing countries of the region have significant capacity for vaccine trials and manufacturing. In section 4.4, we also shed light on public, private, and philanthropic sources of vaccine R&D financing in Asia and the Pacific, on PDPs, and on recent innovations in the financing space. In section 4.5, we made the case for increased investment in vaccine R&D in the region, based on the high cost of inaction and the enormous health and economic benefits of scaling up such financing.

What are the options for such scaled-up financing? In this section, we lay out several mechanisms through which vaccine R&D in Asia and the Pacific could be better financed. We organize these into resource mobilization, pooling of resources, and strategic purchasing (Figure 4.2).
4.6.1 Resource Mobilization

**Governments** in Asia and the Pacific could increase their investments, either into their own domestic R&D enterprise if it is mature enough—several countries have significant trials and manufacturing capacity but are spending very little on vaccine R&D—or into new regional mechanisms (discussed later). Increased domestic financing on developing vaccines for neglected and emerging infectious diseases would reap major public health gains while generating large economic returns. The global movement toward universal health coverage has included a call for greater investment in health research—this movement provides a window of opportunity for governments in Asia and the Pacific to commit a percentage of their domestic health budgets to R&D, including vaccine R&D.

One mechanism that previously has been proposed for mobilizing additional government funding is an **R&D tax** (Rottingen and Chamas 2012), such as allocating 0.01% of gross domestic product toward product development to combat neglected diseases, which could be explored for Asia and the Pacific. There is precedent for using taxes to raise funds for global health: UNITAID mobilized over $2 billion for HIV, TB, and malaria control through an **airline ticket levy** (a “solidarity tax”) (KFF 2011). In the 29 countries that joined the scheme, including the Republic of Korea, a small levy was added to the price of airline tickets.
The Republic of Korea is also using a similar airline solidarity levy to support the Global Disease Eradication Fund.³ An analysis by Song and Pyun (2022) of the country’s airline ticket solidarity levy suggests that this system could be extended to support vaccine R&D and adopted by other countries in Asia and the Pacific to create “sustainable finance schemes.” Other types of taxes have been proposed for mobilizing R&D finance in the region, such as a tax on financial transactions, foreign exchange transactions, or the sale of shares, bonds, and derivatives.

An alternative to an R&D tax would be a voluntary regional earmarked mechanism for vaccine R&D. An example of such a voluntary mechanism is CEPI, which has shown proof of principle as a global mechanism. There would be value in exploring the feasibility of and appetite for a “CEPI for the Asia and the Pacific region.” Such a voluntary earmarked mechanism might also attract additional funding from donor agencies. If donors worked more closely with experts in disease-endemic low- and middle-income countries in Asia and the Pacific to identify vaccine R&D priorities, this could help to address the documented mismatch between global and national research priorities (Viergever 2013). Another way for donors to help support governments in the region to invest more in vaccine R&D would be through a matching fund—in other words, donors could agree to match country investments.

Multilateral funders have shown increased interest in recent years in funding global public goods (GPGs) for health, including global health R&D. Our own recent policy analysis, which examined the role of intensified multilateral cooperation on GPGs for health, argued that “in the current climate of growing worldwide nationalism and populism, the multilateral institutions now find themselves well positioned to become a countervailing force in taking international collective action and supporting GPGs for health” (Center for Policy Impact in Global Health 2018).

As shown in Tables 4.3 and 4.6, industry has made minimal investment into vaccine R&D in Asia and the Pacific—just $14.7 million for neglected disease vaccine R&D and $0.14 million for emerging infectious disease vaccine R&D from 2018 to 2020. This amount represents a tiny fraction of total private sector investment into neglected disease product development. The G-FINDER 2021 report (Chapman et al. 2022) found that in 2020 the private sector invested $491 million in neglected disease basic research and product development (or 12% of global funding). Multinational pharmaceutical companies were responsible for 90% of

Philanthropic investors have not yet made large-scale, sustained investments into vaccine R&D in the region. Several philanthropies have made small contributions to R&D more broadly—not specifically vaccine R&D—which suggests that attracting philanthropic support for vaccine development may be possible. Key informants argued that a pool of sustained philanthropic funding could create a legacy in the region, supporting innovative platforms and serving regional needs.

As Yamey et al. (2018) previously argued, “the public and philanthropic sectors should continue to expand successful incentive mechanisms and test new ones to attract industry to participate in product development for neglected diseases.” Beyond traditional push and pull incentives (e.g., public investments into translational research, advance purchase agreements), newer approaches should also be tested. One example is the Life Prize, “which combines upfront grants with pooling of intellectual property into a patent pool” (Yamey et al. 2018).

### 4.6.2 Pooling of Resources

Interest is growing among funders in developing innovative approaches to global health R&D, including new pooled financing mechanisms. For example, we conducted a study to assess the appetite among funders for a global funding platform—an “ aggregator”—for funding late-stage clinical trials (Yamey et al. 2020). We interviewed 192 relevant stakeholders worldwide and found widespread buy-in for the idea of a new pooled fund. Key informants argued that they would be more likely to participate in a pooled fund if it:

(i) provided financial support for clinical trial capacity in low- and middle-income countries;

(ii) brought domestic commercial benefits to these countries through local manufacturing, ownership of intellectual property, and free licensing;

(iii) led to wide availability of low-cost products in these countries;

(iv) facilitated global knowledge sharing; and

(v) promoted “an equal partnership between Northern and Southern countries across all dimensions, e.g., participation in global governance structures, data ownership, and trial leadership (making sure, for example, that trials have principal investigators from the Global South).”

Another example of a pooled R&D fund proposal, developed by the Center for Global Development, is the proposal to use pooled financing
to incentivize the development of urgently needed new TB tests, drugs, and vaccines (Silverman 2019). The proposed pool, called the Market-Driven Value-Based Advance Commitment (MVAC), would be financed by MICs, especially those with a high TB burden. In the MVAC, MICs would make pooled commitments to purchase new TB technologies, providing guarantees of a market to pharmaceutical companies for newly developed products. The idea is that MICs would commit to purchase new TB technologies by supporting an up-front pool of funding, thus “providing guarantees of a market to pharmaceutical companies for newly developed products” (Yamey et al. 2019).

This type of pooling could be established at a regional level. It would be valuable to explore the appetite for and feasibility of a new pooled R&D vaccine fund for Asia and the Pacific. Such a pooled approach would be especially valuable if it also served as a coordination platform. Such a platform could not only help to mobilize funding, but also support priority-setting processes and transparency about investment decisions. A coordination platform for vaccine R&D in Asia and the Pacific could serve as a kind of “one-stop shop,” informing existing and new public, private, and philanthropic investors about “R&D needs, candidate products in the pipeline, estimated development costs and financing gaps, likely markets, and expected health and economic benefits” (Yamey et al. 2018).

Beyeler and colleagues (2019) in a policy analysis titled “Improving resource mobilization for global health R&D: a role for coordination platforms?” argued that R&D coordination platforms should have four key functions: “building consensus on R&D priorities; facilitating information sharing about past and future investments; building in accountability mechanisms to track R&D spending against investment targets and curating a portfolio of prioritized projects alongside mechanisms to link funders to these projects.” Their analysis also suggested that several design features would maximize success, such as making sure there is a strategy for sustainably funding the platform’s secretariat, separating out the coordination from the financing functions, and including multiple diseases. CEPI and the Global Research Collaboration for Infectious Disease Preparedness (GloPID-R) have shown the value of establishing research priorities across multiple diseases. The risks of launching a coordination platform for just a single disease include creating “a fragmented funding environment where platforms compete for limited funds” (Beyeler et al. 2019) and missed opportunities for basic science investments with benefits across multiple diseases.
4.6.3 Strategic Purchasing

Finally, we have previously noted that “several global health agencies have progressively developed a ‘strategic purchasing’ function through the development of prioritization models to allocate their funding” (Yamey et al. 2019). For example, Gavi allocates about 20% of its funding to support GPGs for health, such as market shaping and pooled procurement (Jamison et al. 2013). The Global Fund’s 2017–2022 strategy included $194 million for “Strategic Initiatives,” many of which were GPGs for health, such as pilot studies of malaria vaccine introduction. This trend suggests that there may be a role for the Asian Development Bank to support regional GPGs for health, including vaccine R&D, building on the bank’s support for APVAX.

References


5
Implementing Flexibilities of Trade-Related Aspects of Intellectual Property Rights to Spur Vaccine Production

Andrew D. Mitchell, Antony Taubman, and Theodore Samlidis

5.1 Introduction

Manufacturing capacity for key vaccine technologies for coronavirus disease (COVID-19) and other diseases remains highly concentrated in a handful of countries. Many observers attribute inequitable and delayed distribution of vaccines at least partly to unevenly distributed production. Along with other factors, such as sustainable financing, regulatory clearance, and logistical capacity, expanding and diversifying vaccine production entails leveraging access to technology platforms such as novel mRNA technologies, viral vectors, and recombinant protein vaccines (WHO 2022). In turn, working such technologies entails access to various inventions, know-how, and regulatory data as part of a broader technology transfer process. Much of this subject matter is protected by intellectual property (IP) rights across multiple jurisdictions (Chiang

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1 This chapter is based on research that was commissioned and supported by funding from the United Nations Economic and Social Commission for Asia and the Pacific. It also draws on the authors’ article, “Intellectual Property and Vaccine Manufacturing: Utilising Existing TRIPS Agreement Flexibilities for COVID-19 and Other Public Health Crises” (2023) 25 Tulane Journal of Technology and Intellectual Property 1. The authors thank Kathrin Rüegsegger for her research assistance. The views and opinions expressed in this chapter do not in any way necessarily reflect those of the authors’ respective organizations; in particular, no view or interpretation in this chapter can be attributed to the World Trade Organization, its Secretariat, or its Members.

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and Wu 2021). Content protected by copyright and industrial design rights may also come into play. A practical response to the COVID-19 pandemic and future potential health crises requires closely mapping the current and projected future needs of various jurisdictions, diversifying production and distribution centers accordingly, and overcoming any IP barriers to such diversification.

Governments and intergovernmental organizations have partly directed their pandemic response toward strategies for leveraging access to critical IP through a range of mechanisms, including promoting voluntary licensing, creating technology sharing platforms such as the World Health Organization (WHO) COVID-19 Technology Access Pool (C-TAP), humanitarian licensing programs such as the Medicines Patent Pool (MPP), targeted technology transfer initiatives, and various means to curb or remove the exclusive effect of applicable IP rights.

For members of the World Trade Organization (WTO), curbing or removing the exclusive effect of applicable rights would normally entail working within the framework of the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). This chapter presents an overview of TRIPS flexibilities and their practical use, and then discusses the scope for their implementation within the broader set of policy tools to spur vaccine production.

Our review addresses a representative sample of countries in Asia and the Pacific, including developing and least-developed countries (LDCs): Bangladesh, Cambodia, Fiji, India, Indonesia, Malaysia, Mongolia, Nepal, Thailand, and Viet Nam. We selected these countries to illustrate different economies’ distinct potential roles in building more diverse vaccine production capacity: some may serve as regional hubs for vaccine production, others may play an intermediate role in the production of vaccine inputs and regulatory approval processes, while others would more likely seek to import vaccines. Ultimately, diverse countries may have common interests in coordinated or pooled procurement and regulatory coordination or convergence to expedite and streamline regional access to vaccines.

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4 For details on MPP’s contribution to the global response to COVID-19, see MPP web page at https://medicinespatentpool.org/covid-19.

5 See, e.g., ASEAN (2016).
5.2 TRIPS Flexibilities

The TRIPS Agreement, a multilateral trade agreement concluded as an annex to the Agreement Establishing the WTO, primarily sets down a “floor” of positive, minimum standards or general principles for how national systems protect IP in WTO members. These principles cover the eligible subject matter, the consequent rights, and the manner of their enforcement. In imposing these obligations, TRIPS, explicitly and implicitly, leaves room for maneuver or flexibility for WTO members, allowing them to go beyond the minimum standards imposed, and confirming scope for exceptions and limitations according to general principles. The Declaration on the TRIPS Agreement and Public Health (Doha Declaration, WTO 2001) clarified and affirmed several policy options or “flexibilities” open to WTO members to leverage access to pharmaceuticals, and paved the way for a public health amendment to the treaty. In applying these flexibilities, some governments have raised concerns that even when taking legitimate, TRIPS-compliant measures, they may be subject to political and economic pressure by major trading partners and the private sector. Such pressures can be alleviated by strengthening national governments’ agency in addressing the IP dimension of enhanced and sustainable vaccine production (Taubman 2022).

TRIPS does not in itself establish domestic IP systems, and members must give effect to its principles and standards through domestic laws and regulations. It is integral to TRIPS implementation that members apply TRIPS standards within their national legal regimes and judicial and administrative systems, adapting to national needs and circumstances, while these systems remain compliant and consistent with treaty standards, which are more general in character to domestic legislation. Thus, the benefits of flexibilities are only realized through applied choices in the framework of WTO members’ domestic laws, along with some regional IP systems.

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6 TRIPS art 1.1.
7 These identified “flexibilities” are only illustrative and not exhaustive of the potential TRIPS-compliant policy options that members can take. The World Intellectual Property Organization (WIPO) has identified four clusters of TRIPS flexibilities, relating to the method of implementing TRIPS obligations; substantive standards of protection; mechanisms of enforcement; and areas not covered by the TRIPS Agreement (see WIPO web page on public policy-related assistance – flexibilities at https://www.wipo.int/ip-development/en/policy/flexibilities.html).
8 WIPO (2010), 8 [23].
Given their distinct needs and circumstances, LDCs have benefited from successive transition periods and will not be required to apply substantive TRIPS standards until at least July 2034. Among the surveyed countries, this applies to Bangladesh, Cambodia, Nepal, and Myanmar, which retain broad latitude under TRIPS to adapt IP laws to address the pandemic and future health crises. Thus, in principle, there would be no legal obligation under TRIPS that would constrain an LDC with sufficient industrial base (such as Bangladesh, which has a vibrant pharmaceutical industry) from producing generic medicines to meet national demand and to export to countries where no relevant patent is in force or a nonvoluntary use authorization applies, provided the necessary technical and manufacturing capacity can be established for the specific medicines concerned (Mahmud-Al-Rafat et al. 2022; Rahman and Farin 2018).

### 5.2.1 Patents

A patent confers on its owner the exclusive right, within the relevant domestic jurisdiction, to make, use, sell, and import the invented product or process specified in the patent. Vaccines and processes for their production are generally subject to the protection of one or more patents. Thus, in principle, a firm could not produce vaccines without the patent holder’s consent in those countries where relevant patents are in force. Equally, patent rights can prevent the importation of finished vaccines or inputs for their production, where this occurs without the patent holder’s authorization. Patents for technologies and devices applied to administer vaccines (Stevens et al. 2017) and technologies used for storage and delivery may also need to be addressed to ensure effective vaccine access.

Patent applications are generally published 18 months after the first filing date, ensuring technological information enters the public domain early in the vaccine development process. And the strictly territorial scope of patents under national and regional systems means that an invention passes immediately into the public domain and is free from exclusive rights in those jurisdictions where a patent is not sought.

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10. Patent Analytics Hub identifies 1,422 applications and 290 unique patent families filed globally since 2000 relating to human coronavirus vaccines, with 50% of these patent families either being sought or in force (IP Australia 2020). See also Gaviria and Kilic (2021).
typically the majority of developing countries.\textsuperscript{11} Thus, patent mapping is a critical practical consideration in establishing freedom to operate in charting options for access to medicines. The key impediment to utilizing an invention in cases where an invention is known but not protected is obtaining the necessary technical information to carry out the invention. In principle, a patent document must fully teach the person skilled in the art how to implement the invention,\textsuperscript{12} and a patent can be invalidated for insufficient disclosure. However, further know-how is typically needed to effectively use patented technology, especially in the complex area of pharmaceutical technology, where it is difficult to replicate or reverse engineer detailed manufacturing know-how.

In those countries where a patent is in force, governments have considerable scope to override its exclusive effect in the public interest. These flexibilities are discussed in the following subsections.

### A. Patentability

Article 27 of the TRIPS Agreement requires members to make patents available for any inventions—whether products or processes, which are “new,” “involve an inventive step,” and are “capable of industrial application.”\textsuperscript{13} While these terms are not defined by TRIPS itself, it does clarify that “inventive step” and “capable of industrial application” can be considered synonymous with “non-obvious” and “useful,” respectively, and “novel” is also often used as a synonym for “new.” It follows that WTO members have considerable latitude in determining the application of these terms, in their domestic patent laws, through judicial decisions and in examination guidelines applied by patent granting authorities.

The threshold question is the definition of an “invention,” and there are varied practices among WTO members. For example, Fiji’s patent law defines an invention as “any manner of new manufacture and every new process of manufacture and every new method of application of known processes and improvements in any known process.”\textsuperscript{14} Thailand includes under its definition “any improvement of a known product or

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\textsuperscript{11} According to data by the WIPO IP Statistics Data Center (www3.wipo.int/ipstats/, accessed 15 December 2021), approximately 47% of 3,276,700 patent applications filed in 2020 were filed in high-income countries, 46% in the People’s Republic of China (PRC), and only 7% in low-income and lower middle-income countries (excluding the PRC). In 2021, the number of patent applications filed in low-income countries fell to 8,600, compared with 1.57 million in high-income countries.

\textsuperscript{12} TRIPS art 29.1.

\textsuperscript{13} TRIPS art 27.1.

\textsuperscript{14} Laws of Fiji, Chapter 239, Patents (Fiji) s 2 (Fijian Patent Law).
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process.”\textsuperscript{15} Indonesia’s definition expressly excludes a “discovery in the form of: ... new use of existing and/or known product; and/or new forms from existing compound which does not generate significantly enhanced efficacy and contains different relevant known chemical structures to compound.”\textsuperscript{16}

Article 27 provides for domestic policy choices in terms of permissible exclusions from the scope of patentable subject matter that may be relevant to pharmaceutical technologies, in particular “diagnostic, therapeutic and surgical methods for the treatment of humans or animals.” However, even if broadly construed, such methods do not really include processes and inputs for producing vaccines, nor the finished vaccines themselves. Article 27.3 is concerned only with methods for treatment, which would arguably be limited to processes for the final administration of vaccines (should these be claimed as potentially patentable inventions).

This exclusion is applied in a number of countries in Asia and the Pacific.\textsuperscript{17} India goes further by excluding from patentability “any process for the medicinal, surgical, curative, prophylactic, diagnostic, therapeutic or other treatment of human beings.”\textsuperscript{18} By excluding “prophylactic ... treatment” from patentability, India’s provision may possibly exclude methods for actual administration of vaccines, which are not expressly encompassed within the methods of treatment specified in Article 27.3.\textsuperscript{19} In any case, this does not exclude vaccines as such, since these products are clearly distinct from processes or methods for the prophylactic treatment of human beings.

B. Patent Disclosure

A long-standing, central principle of patent law is that the invention must be fully disclosed in sufficient detail for a skilled person to put the technology into effect. Patent disclosure is at the heart of the patent


\textsuperscript{16} Law of the Republic of Indonesia No. 13 of July 28, 2016, on Patents (Indonesia) s. 4 (Indonesian Patent Law).

\textsuperscript{17} See, e.g., Law on Patents, Utility Models and Industrial Designs (Cambodia) art 9(iii) (Cambodian Patent and Designs Law; Patent Law of 25/06/1993 (Mongolia) art 4.7.5 (Mongolian Patent Law); Patents Act No. 291 of 1983 (Malaysia) s 13(d) (Malaysian Patent Law); Thai Patent Law (n 19) s 9(4); Indonesian Patent Law art 9(b).

\textsuperscript{18} Patents Act, 1970 (India) s 3(i) (Indian Patent Law).

\textsuperscript{19} See also, Thai Patent Law (n 19) s 9(4); Indonesian Patent Law (n 20) art 4(f).1, which states “any method.”
function: it permits interested parties to use the patented technology in return for the patentee gaining a defined period of market exclusivity over the invention (Lu 2012). In principle, the protected technology must pass fully and effectively into the public domain. The ready availability of patent information online assists in making full use of the technology in those countries where the patent has not been applied for, typically the majority of developing countries. Thus, this mechanism can affect firms’ ability to engage in technology transfer, including enabling an early review of available technologies still undergoing development, even before exploring licensing possibilities.

Article 29 obliges members to require patent applicants to disclose the invention “in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art.” The Article also permits but does not compel members to require patent applicants to “indicate the best mode for carrying out the invention known to the inventor at the filing date or, where priority is claimed, at the priority date of the application.” In the view of Carlson, Przychodzen and Scamborova (2005), this best mode requirement acts as the “linchpin ... of the patent system,” ensuring that the invention is properly disclosed and, when appropriate, can be properly worked.

Our survey indicates that the laws of Cambodia, India, Malaysia, Mongolia, and Thailand require the best-known mode to be disclosed, while those of Bangladesh, Fiji, Indonesia, Nepal, and Viet Nam do not. Failure to meet disclosure requirements leaves a patent open to revocation, or a reduction in the scope of the patent claims.

C. Exceptions to Patent Rights

Article 28 requires members’ domestic laws to afford patent owners the right to exclude others from making, using, offering for sale, selling, or importing patented products or products produced by a patented process, and from using a patented process. However, these “exclusive rights” are not absolute. It is well established that they may be curtailed or overridden for the public interest or the legitimate interests of third

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20 TRIPS art 29.1.
22 Indian Patent Law s 4(b).
23 Patent Regulations 1986 (Malaysia) r 12(e).
24 Mongolian Patent Law (n 20) art 7.3.1.
25 Thai Patent Law (n 19) s 17(3); Ministerial Regulations No. 21 (B.E. 2542) issued under Thai Patent Law r 3(6).
parties, such as researchers and other firms. Articles 30, 31, and the related 31bis specify two broad classes of such exceptions and limitations to the rights provided for in Article 28. The following subsections review only those Article 30 exceptions most relevant to vaccine production and distribution.

**Regulatory Review Exception**

To obtain regulatory approval to place a follow-on pharmaceutical product on the market, a generic producer may need to use the originator’s patented technology.\(^{26}\) In principle, this would violate the Article 28 right to exclude the “use” of the patented technology. Yet, delaying such regulatory use until a patent expires or lapses would unreasonably extend the effective term of the patent. Hence, it is in the public interest that regulatory processes be concluded by the time the patent term expires so that the generic producer can enter the market quickly and enhance access to the patented medicine.

Following WTO dispute settlement on the matter,\(^ {27}\) it is now widely accepted that such use is a legitimate exception under Article 30, generally termed a regulatory review or “Bolar exception”: examples from our survey include the laws of India,\(^ {28}\) Malaysia,\(^ {29}\) and Viet Nam.\(^ {30}\) This exception provides one avenue for accelerating market entry for generic pharmaceutical products, thus potentially diversifying production and reducing prices through competition. In particular, it may reduce the delay between a patent’s expiry and the ability of local manufacturers to exploit the vaccine by producing and selling it domestically. However, this only comes into play when a domestic regulatory authority requests data based on the use of the patented technology in the course of approval of the follow-on generic product. This may not be the case, for instance, where products can be approved based on regulatory clearance in other jurisdictions. It is only necessary where there is a patent in force over a vaccine that a domestic producer wishes to manufacture, and no other flexibilities have been or will be utilized to provide the local producer with access to relevant IP in the invention before the patent term expires.

\(^{26}\) For instance, by producing sufficient quantities of the medicine to demonstrate its safety and efficacy or equivalence to the original product.

\(^{27}\) Canada — Pharmaceutical Patents (DS114).


\(^{29}\) s37 (1A), Patents Act 1983.

\(^{30}\) Art 125 (2) (a), Intellectual Property Law No. 50/2005/QH11.
Research and Other Exceptions

The most significant exceptions for access to medicines are for research and analysis, and for pharmacists to make up prescribed medicines. Generally, it is accepted that researchers can use a patented invention for investigation, study, and experimentation (Taubman, Wager, and Watal 2020), including for determining whether the invention produces the results claimed for it, provided this stops short of commercial exploitation. Research exceptions are likely to assist countries in undertaking relevant preparatory research and analysis but would not alone permit the manufacture or sale of vaccines. Equally, for public policy reasons, a pharmacist can make up a patented medicine on the prescription of a medical practitioner, without the patent holder’s consent, but this does not apply to large-scale vaccine production and distribution. The research exception has been expressly implemented in the laws of Mongolia, Thailand, India, and Indonesia.31 However, such an exception may be allowed by the courts based on the broader principles of patent law, including as an exception to the remedies available for alleged patent infringement. That said, an express exception in domestic legislation would provide clarity and confidence to those seeking to use this legitimate option and avoid the uncertainty and delay of litigation.32

D. Government Interventions to Safeguard Public Health

Member governments have considerable agency to override the exclusive effect of patent rights in the public interest, notably to protect public health. This includes an array of legal measures to authorize the use of patented subject matter, whether directly by government agencies, on behalf of governments, or by third parties, without the consent or involvement of the patent holder. These interventions are often collectively termed “compulsory licenses” but may also be more accurately denoted “nonvoluntary use authorizations” (NVUAs), as such measures may take different forms from a specific license, such as government use orders and emergency decrees (Taubman 2008a).

Compulsory licenses and other NVUAs can be issued on various grounds and for various policy reasons. These fall into two broad categories:

(i) compulsory licenses that aim to preserve a healthy state of competition between firms, promote more competitive use of patented technology, or remedy anticompetitive practices, and

31 See, e.g., Mongolian Patent Law (n 20) art 18.2.2; Indian Patent Law (n 20) s 47(3); Indonesian Patent Law (n 201) arts 6(1)(b), 19(3); Thai Patent Law (n 19) s 36(1).
32 See, e.g., Thai Patent Law (n 19) s 36(2) and s 36 (3).
(ii) other public interest NVUAs that directly permit the use of patented technology for public noncommercial purposes, for emergencies, in cases of extreme urgency or directly in the public interest, regardless of the competitive environment.

When it comes to pursuing large-scale production of medicines without the right holders’ authorization, whether for domestic or export purposes or both, the first avenue is to explore the full scope of mechanisms available under Articles 31 and 31bis, as well as the waiver of Article 31(f) established by the 12th Ministerial Conference's Decision on the TRIPS Agreement (WTO 2022). The practical implementation of such measures can be streamlined and made more effective, including through simplifying and clarifying procedures, aggregating demand to build economies of scale, and using complementary options to address regulatory processes. The following subsections look more closely at the basic elements required to successfully apply compulsory licenses in practice.

**Grounds for Authorization**

The substantive grounds for issuing a compulsory license are left open in TRIPS, as WTO members have expressly clarified, meaning that a government can provide any number of bases for the authorization of nonvoluntary use.

The ground most frequently specified is a failure to work the invention in the relevant country’s territory, reflecting the Paris Convention provision that confirms “the right to take legislative measures providing for the grant of compulsory licenses to prevent the abuses which might result from the exercise of the exclusive rights conferred by the patent, for example, failure to work.” Another related ground arises when demand is not being met, or not being met on reasonable terms.

Grounds for invocation lacking in some domestic regimes which may be useful in the pandemic context include (i) public health or public interest, (ii) refusal to deal, and (iii) general government or public noncommercial use. The patent laws of Cambodia, India, Indonesia,

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33 See Doha Declaration (8) para 5(b); also Taubman (2008) and WTO (2020).

34 See, e.g., Malaysian Patent Law (n 20) s 49(1)(a); Indian Patent Law (n 21) ss 84(1)(c); Cambodian Patent and Designs Law (n 20 art 56).

35 Article 5 A(2), Paris Convention for the Protection of Industrial Property (as amended on 28 September 1979).

36 The Patents and Designs Act, 1911 (Bangladesh) (n 20) s 22(1) (Bangladesh Patent and Design Law); Indian Patent Law (n 21) s 84(7).
Malaysia, Mongolia, Thailand, and Viet Nam provide grounds based on public interest, public health, or other emergency circumstances. Some countries, such as Malaysia and Thailand, include a public interest or national emergency ground in their laws by incorporating Article 31(b). Article 31(b) sets a refusal to issue a voluntary license as a precondition to granting a compulsory license. However, this does not apply to emergency or public use contexts, and overriding the need first to seek a voluntary license would streamline the application process in a public health crisis. Further, refusal to license on reasonable terms can be made out to be a ground in itself for a compulsory license (Correa 2005) and is expressly set out as such in the laws of several countries. It may also be the basis of a finding of anticompetitive practice that a compulsory license could remedy.

Of the countries surveyed, only India’s and Viet Nam’s laws expressly provide for this ground. It is also identified as a potential ground of abuse within India’s anti-competition provisions relating to abuse of dominant position. It may also be implicit in some countries’ ground of “demand not being met on reasonable terms.” That said, in principle, a patent holder has no fundamental or unconditional obligation to refuse a license.

**Forms of Authorization**

Article 31 is carefully framed to give scope for various measures within domestic legal systems and its implementation is not limited to any specific mechanism, such as a compulsory license issued in response to an application. Hence, reflecting widespread practice, it is plainly envisaged that a government may directly authorize the use of a

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37 Cambodian Patent and Designs Law (n 20) art 47(i): “the public interest, in particular, national security, nutrition, health or the development of other vital sectors of the national economy so requires”; Indian Patent Law (n 21) ss 84(1)(a), 84(2); Indonesian Patent Law (n 20) art 82(1); Malaysian Patent Law (n 20) s 84(1); Mongolian Patent Law (n 20) art 20; Thai Patent Law (n 19) ss 51, 52; Law on Intellectual Property (No. 50/2005/QH11) (Viet Nam) arts 133, 145 (Vietnamese Intellectual Property Law).

38 Malaysian Patent Law (n 20) s 84; Thai Patent Law (n 19) ss 51, 52.

39 See Anderson, Taubman, and Carvalho (2021, 857); also, e.g., the laws of Egypt and Viet Nam, discussed in WIPO (2013, 9).

40 Indian Patent Law (n 20) s 84(7)(a); Vietnamese Intellectual Property Law (n 41) art 145(c), establishing as such a ground “failure to reach agreement on a licence in spite of efforts made within a reasonable time for negotiation on satisfactory commercial price and conditions” (WIPO translation).

41 Unlike other provisions in India’s competition law, these provisions are not subject to an IP exemption (Anderson et al. 2021).

42 See WIPO (2013), (n 44).
technology for public use—and a fortiori in an emergency or situation of urgency—without seeking to identify relevant patents in advance. This means that a government contractor is not expected to carry out a patent search but is obliged to inform a patent holder if there is knowledge or demonstrable grounds to know that a valid patent is involved. This understanding is critical to addressing two major concerns that have been voiced concerning the use of NVUAs to overcome exclusive rights in the COVID-19 pandemic:

(i) that a burdensome process of searching for and identifying relevant patents must be undertaken prior to any NVUA being issued, and

(ii) that a multitude of distinct NVUAs must be ordered one by one for each patent.

Neither is the case. No application for compulsory license is required in such circumstances. The context in which an application may be required from a practical perspective is when a private firm wishes to use a patented technology in a commercial context and encounters a patent barrier. Of the countries surveyed, many have reserved the right to authorize the use of patented subject matter separately from any distinct application by a third party. For instance, under Cambodia's patent law, “the Minister may decide that, even without the agreement of the owner of the patent, a Government agency or a third person designated by the Minister may exploit the invention.” Similarly, Indonesia's laws authorize “the government itself” to exploit a patent (including through authorization of a third party) “[i]n the case that the government is in the opinion that a patent in Indonesia very important for state defense and security” or “there is an urgent need for the public interest of a patent.” In Malaysia, the minister may decide that, even without the agreement of the patent owner, a government agency or a third person designated by the minister may exploit a patented invention. The minister's decision-making power is enlivened where there is “national emergency or where the public interest … so requires” or “where a judicial or relevant authority has determined that the manner of exploitation by the [patent owner] … is anti-competitive.”

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43 See, e.g., Industrial Property Act No. 19 of 1994 (Tonga) s 13(5)(a).
44 Cambodian Patent and Designs Law (n 20) art 47.
46 Malaysian Patent Law (n 20) s 84(1).
The Decision on the TRIPS Agreement adopted by the 12th Ministerial Conference expressly clarified that governments can authorize “use of subject matter of a patent under Article 31 without the right holder’s consent through any instrument available in the law of the Member such as executive orders, emergency decrees, government use authorizations, and judicial or administrative orders, whether or not a Member has a compulsory license regime in place.” It clarified that the reference to the “law of a Member” in Article 31 “is not limited to legislative acts such as those laying down rules on compulsory licensing, but it also includes other acts, such as executive orders, emergency decrees, and judicial or administrative orders.”

“Individual Merits”: Article 31(a)

Article 31(a) requires that the “authorisation of such use shall be considered on its individual merits.” There are concerns that subparagraph 31(a) requires each individual patent license to be considered and granted on its individual merits, that is, on a case-by-case basis, thus posing a potential obstacle to the expeditious use of options under Articles 31 and 31bis. However, this provision requires that each authorization to use patented subject matter be considered on its individual merits, (rather than each authorization to infringe a distinct patent). Thus, there is scope for approval relating to a package of technology (which may entail multiple patents held by distinct owners) and for multiple authorized users. A government body issuing a compulsory license or use order need only authorize the use of a given vaccine and its manufacturing process once. Article 31(a) may preclude governments from preemptively compulsorily licensing a whole category of multiple patents relating to a particular subject matter or industry (Taubman, Wager, and Watal 2020). Still, it entitles a government directly to authorize the production of a specified vaccine in a single step, regardless of the potential complexity of the patent landscape and without a prior patent search and without previous notice to or negotiation with patent owners. Beyond the scope of our review, more elaborate implementation of such measures can be found in the form of extensive mechanisms for direct government authorization, such as “Crown use” in the United Kingdom, and limitations on remedies for infringing government use, as is provided in the United States.

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47 See WTO (2022), fn 42 supra.
48 See, e.g., WTO (2021a) and Lo (2017).
50 United States Code, Supplement 5, Title 28 - Judiciary and Judicial Procedure s1498.
Implementing Flexibilities of Trade-Related Aspects of Intellectual Property Rights to Spur Vaccine Production

Consistently also with Article 44(2) of TRIPS (which itself is modeled on practice in the United States).

Prior Efforts to Obtain Authorization: Article 31(b)

Under Article 31, TRIPS sets requirements for a proposed user of patented technology to first seek authorization from the right holder “on reasonable commercial terms and conditions,” and such efforts must be unsuccessful within a reasonable period. However, this requirement does not apply “in the case of a national emergency or other circumstances of extreme urgency or in cases of public non-commercial use,” situations that clearly embrace the response to COVID-19 or other health crises. Hence, in the context of a pandemic response, there is no requirement to seek prior approval from a patent holder to produce vaccines without their authorization. This requirement in domestic laws could be relaxed while remaining consistent with TRIPS.

When licensing negotiations are required, it may be helpful to consider the TRIPS principles that may apply where domestic law maintains a requirement first to seek the patent holder’s authorization. Members have considerable scope to determine their own standards and mechanisms for applying the TRIPS standards in particular cases (Mitchell and Voon 2009), including what amounts to reasonable licensing terms and period of time.

Surveyed members’ laws vary considerably (Kampf 2015) when explicitly specifying the “reasonable period of time” that is sufficient for determining whether efforts to obtain the patentee’s authorization have been unsuccessful, ranging from 21 days (Cambodia) to 12 months (Indonesia). India specifies 6 months but merely includes the requirement of unsuccessful efforts within a “reasonable period time” as a factor to be considered in determining whether a license should be granted. Particularly in situations where the public interest requires a more rapid determination of whether a NVUA is granted, it may be possible to adapt the period appropriately in line with members’ practice.

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51 TRIPS art 31(b).
52 Law on Compulsory Licensing for Public Health (Cambodia) art 9 (Cambodian Compulsory Licensing Law).
53 Indonesian Patent Law (n 20) art 84(l).
54 Indian Patent Law (n21) ss 84(6)(iv), (v).
Scope and Duration Limited: Article 31(c)

Article 31(c) limits the scope and duration of use to the purpose for which such use was authorized. Some members impose a general time limit on the term of compulsory licenses (Ng and Kohler 2008). The words “limited to the purpose for which it was authorised” in Article 31(c) indicate that the duration is determined with reference to the purpose of the use; hence, members need not limit the duration according to a particular chronology.

Concerning scope of authorized use, some developing countries only provide for authorized manufacture, not importation (Correa 2005). This could impede several legitimate avenues for access by members, especially those reliant on imports for medical needs—namely, importation from a jurisdiction where no patent is in force, where a conventional NVUA provides for a proportion of production to be exported, or where production for export is authorized in line with the Article 31bis system.

Predominantly for the Supply of the Domestic Market: Article 31(f)

The requirement that use be authorized predominantly for the supply of the domestic market of the member authorizing the use previously meant that a country with little or no manufacturing capacity could not receive pharmaceuticals produced and imported under a compulsory license in another country that did have such capacity. Article 31bis, discussed later, now addresses this issue.

Hypothetically, this requirement implies that it would be open to India, for instance, with a domestic population of almost 1.4 billion, to authorize production of a vaccine or other pharmaceutical predominantly for its domestic needs, and for that production also to be authorized for distribution to all other South Asian countries (with a combined population of 470 million) and all Association of Southeast Asian Nations member states (with a combined population of 660 million). There would be no need to consider alternatives to Article 31(f) because the non-predominant proportion of India’s production would be for the supply of foreign markets.

Continued Existence of Circumstances Which Led to Authorization: Article 31(g)

Article 31(g) provides that the authorization “shall be liable, subject to adequate protection of the legitimate interests of the persons so authorised, to be terminated if and when the circumstances which led

55 This would be the case where a “predominant” proportion of the demand for the product was from other members rather than the domestic market.
to it cease to exist and are unlikely to recur” and that the “competent authority shall have the authority to review, upon motivated request, the continued existence of these circumstances.”

This provision does not require that the authorization be terminated if and when the relevant circumstances have ceased to exist and are unlikely to recur. Rather, it requires that persons within a member’s jurisdiction have the opportunity to petition its termination on such grounds.

**Adequate Remuneration: Article 31(h), (j)**

What can be considered as adequate remuneration? While practice varies considerably as to the exact level of remuneration, common figures run from 1% to 2% of the value of production. There is also a strong expectation that remuneration should be adjusted in cases of production for humanitarian purposes.

Remuneration guidelines commissioned by the United Nations Development Programme and WHO recommend that systems for remuneration be easy to administer and “assist rather than defeat” the goal of enhancing access and lowering costs (Love 2005).

India’s patent law requires that remuneration be “reasonable,” having regard to “the nature of the invention, the expenditure incurred by the patentee in making the invention or in developing it and obtaining a patent and keeping it in force and other relevant factors.” Cambodia’s Compulsory Licence Law states that “the production, importation or exportation of the Pharmaceutical Products under a compulsory licence shall be subject to payment of remuneration to the patent holder,” but does not specify the considerations to be taken into account in determining an adequate or equitable amount, leaving it to the relevant ministers to determine the relevant “method” and “criteria” for the rate of remuneration. Indonesia’s law requires the annual patent fee to be paid by the government or the third-party authorized under the license.

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56 TRIPS art 31(g).
57 Bearing in mind, also, that several patents may be relevant to a particular vaccine, and there is no expectation of a one-to-one mapping between individual patents and vaccines.
58 Indian Patent Law (n 20) s 90(1).
60 Indonesian Patent Regulation (n 50) art 11.
Judicial Review: Article 31(i)

Article 31(i) does not prevent a member from giving immediate effect to a compulsory license pending administrative or judicial review, provided that adequate protection of the legitimate interests of the patent holder is assured. Cambodia’s Compulsory Licence Law, for instance, recognizes this by providing that a “competent court shall not issue any provisional measure until a final decision on the case is made.”

There is also no requirement to give a hearing to potentially interested parties, such as the patentee. However, some laws require that the patentee be given a hearing if requested, even in a national emergency or other urgent situations. These provisions may be appropriate for non-emergency use situations. Still, they should be removed from provisions that implement Article 31(b), so that they do not undermine governments’ capacity to urgently authorize the use of medical and other emergency technologies.

Compulsory Licenses for Export: Article 31bis

Article 31bis was introduced into TRIPS to enable a new form of compulsory license or NVUA expressly for the export of pharmaceutical products. Its roots are to be found in the Doha Declaration, which recognized the problem of members with insufficient or no manufacturing capacities in the pharmaceutical sector to make effective use of compulsory licensing. This provision was first implemented as a waiver and then as a formal amendment to TRIPS (the inclusion of Article 31bis with Annex and Appendix). Its potential use arises in practice when the product cannot be produced domestically and the desired manufacturer of the needed product is situated in a country where that product is under patent protection, but a voluntary license is not available (and a lesser proportion of production under a compulsory license in that country is not available for export). To ensure efficient functioning of export licenses expressly for export, Article 31bis introduces three distinct derogations to Article 31. The first is from the obligation in Article 31(f) for the exporting member to supply pharmaceutical products “predominately for the domestic market.” Under certain conditions, which are outlined in the annex to Article 31bis, the exporting member may issue a compulsory license for the export of pharmaceutical products to those countries lacking the manufacturing capacities to produce such products.

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61 Cambodian Compulsory Licensing Law (n57) art 16.
62 See, e.g., Malaysian Patent Law (n 20) s 84(4).
63 WTO (2005), Art 31bis paragraph 1.
The second modifies the obligation under Article 31 to provide “adequate remuneration” to avoid double remuneration. The third derogation facilitates the export of pharmaceuticals to countries within a regional trade agreement, of which half of the members are LDCs, so they can benefit from economies of scale and enhance local production.

Since the NVUA for export only creates a legal pathway for production and export of the needed medicine, it does not by itself address any regulatory requirements in the importing or exporting country or create economies of scale sufficient to support fresh production. One constraint with this mechanism is that it is demand driven. To solve this issue, it is recommended that such authorizations be combined with those for domestic production and export in other countries in need. Hence, it makes sense to address multiple countries’ demand for vaccines and to proceed to pooled or coordinated procurement, and use regional and international mechanisms to coordinate.

So far, very little use has been made of NVUAs expressly for production for export. This has led to considerable critical commentary from WTO members, public health advocates and scholars. Much of this criticism, which has intensified during the pandemic, is leveled at its procedural requirements; it has been called, among other things, a “maze of rules and procedure” (Gupta 2010), “unworkable,” and “unnecessarily complex.”

Article 31bis authorizations could be more effective if integrated into collective procurement programs, which routinely notified expected demand (Taubman 2022). Through a pragmatic approach, including by maximizing flexibilities and strengthening coordination and mutual support among countries, it can be used to good effect (Mitchell, Taubman, and Samlidis 2023).

Generally, the system can be utilized by WTO members to import medicines without any specific steps to implement it domestically, since importation under a compulsory license is already an option in most countries. In many cases, there will be no patent in force. Of the countries surveyed, only India, Indonesia, and Cambodia have provisions expressly implementing some aspect of the Paragraph 6 System. It may

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64 WTO (2005), Art 31bis paragraph 2 2.
65 WTO (2005), Art 31bis para 3.
66 WTO (2021b), 3 [44-45].
67 A full list of WTO members who have notified such legislation to the TRIPS Council or introduced such legislation but not notified it is available at WTO. Members’ Laws Implementing the ‘Paragraph 6’ System. www.wto.org/english/tratop_e/trips_e/par6laws_e.htm
be desirable or constitutionally necessary for other members to adapt their domestic systems to facilitate use of the system.

**Compulsory Licenses and the Article 31(f) Waiver under the 12th Ministerial Conference Decision**

The Ministerial Decision (WTO 2022) did not lead to a waiver of the TRIPS Agreement itself, but merely to a waiver of its Article 31(f). In addition to this waiver, the decision provides for clarifications and simplifications of compulsory licensing for producing and exporting COVID-19 vaccines. The effect of the waiver of Article 31(f) is to provide for a streamlined measure for vaccine production, predominately for export as an alternative to the Paragraph 6 System (Mitchell, Taubman, and Samlidis 2022). One of the key differences in comparison to the Paragraph 6 System is that this option has a supply- rather than a demand-driven character, more adaptable in the uncertain and more volatile circumstances of a pandemic.

Overall, members should ensure that the domestic procedures adopted for implementing Articles 31 and 31bis are as simple, efficient, and transparent as possible. This can be achieved partly by ensuring that additional requirements are not imposed as part of the compulsory license process. Members should also reduce the number of administrative, legislative, and judicial authorities involved in the compulsory licensing process, clearly defining their respective roles and ensuring they pursue policy goals harmoniously,68 particularly where a license is issued in circumstances of urgency. Judicial bodies should be reserved for the role designated to them by Articles 31(i) and (j) and other applicable TRIPS provisions, subject to the requirements of an individual member’s system of government.

Another barrier to the effective use of patents is the disclosure of otherwise secret or confidential information on the use of the invention (Walsh et al. 2021). Compulsory licenses do not ordinarily require the disclosure of such information.

**E. Revocation**

Article 32 of TRIPS provides that “[a]n opportunity for judicial review of any decision to revoke or forfeit a patent shall be available.” Revocation is primarily permitted on the ground of a failure to work within the laws of the countries surveyed.69 India’s law allows the government to revoke a patent where it is “of opinion that a patent or the mode in

68 WIPO (2019), 49.
69 Bangladesh Patent and Design Law (n 40) s 23(1); Indian Patent Law (n 21) s 85; Thai Patent Law (n 19) s 55(1).
which it is exercised is mischievous to the State or generally prejudicial

to the public,” subject to the patentee’s right to be heard.  70 Revocation

can be considered preferable to the procedure under Articles 31 and

31bis where the invention is widely needed, and revocation is the more

administratively efficient option.

5.2.2 Copyright and Industrial Designs

Copyright issues regarding written material on product information
documents, product labeling and inserts, and software and data
compilations utilized in the vaccine manufacturing and distribution
process have been highlighted as problem areas in the pandemic
context.  71 Article 10(2) of TRIPS requires that “compilations of data or
other material … which by reason of the selection or arrangement of their
contents constitute intellectual creations” be protected. As clarified by
Article 9(2), copyright protects expressions, and not ideas. It would not
normally protect individual data items, such as raw statistics. Article 13
of TRIPS makes implicit the availability of exceptions to copyright
protection in certain special cases.  72 In a pandemic context, the two
following permissible exceptions are relevant to vaccine production and
distribution:

(i) exceptions for use by commercial entities of copyrighted
materials necessary but ancillary to vaccine production and
distribution (e.g., product inserts and software); and

(ii) nonvoluntary government or public noncommercial use
(i.e., compulsory licensing of copyrighted material).

Members may overcome any copyright-related obstacles to vaccine
distribution and access by assessing and potentially reviewing the scope
of copyright protection under domestic law for copyrighted material
such as product inserts, which only form an ancillary element of a
product that is the principal subject of production and distribution. It
may also be prudent to review the scope for nonvoluntary government
or public noncommercial use of such materials.

Industrial design protection protects the outward appearance of
manufactured products, but not the product _per se_. Thus, an industrial
design holder has the exclusive right to produce and sell products
incorporating its design. Industrial designs are overall less relevant

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70 Indian Patent Law (n 21) s 66.
71 WTO (2021d), [40]. See also Long (2021).
72 TRIPS art 13.
to the manufacture and distribution of COVID-19 vaccines than the development and distribution of other medical products, such as diagnostic tools, ventilators, and personal protective equipment (PPE).\textsuperscript{73}

Moreover, vaccines are primarily delivered through diluent containers, single-dose and multidose vials, and prefilled syringes, and transported using refrigerators, freezers, and cold boxes. Some jurisdictions have registered industrial designs for items such as vaccine transportation containers, freezers, syringes, and other delivery items. These may be procured at several points throughout vaccine distribution and delivery by private and public entities. However, no specific IP obstacles to access such devices have come to light (in contrast to supply chain scarcity for vaccine inputs generally [WTO, 2021e]).\textsuperscript{74}

In cases where design-related obstacles occur, members can assess and potentially review the applicable domestic law on designs, including a potential exclusion of designs dictated essentially by technical or functional considerations, a requirement of significant difference from known designs or combinations of design features, a limitation of protection of designs in cases of “noncommercial use,” and the possible scope for nonvoluntary government use of protected industrial designs, including based on public health needs.

### 5.2.3 Confidential Information

The protection of confidential or undisclosed information may affect access to knowledge or information necessary to undertake the steps required to produce a vaccine, such as technical methods of production or use of the equipment involved, including their precise settings and arrangement, and biological and other materials used in vaccine development (Gurgula and Hull 2021).

Such information and know-how constitute core components in producing any vaccine, such as tacit knowledge about production methods. While much information required may be in the public domain, some specialist knowledge is more likely to be protected in the context of newer technology platforms, such as mRNA vaccines. Vaccine technologies are best understood as a package of various inputs comprising patented inventions and/or know-how, some of which may be confidential (Van Overwalle 2011). Hence, even if there is no patent

\textsuperscript{73} See, e.g., WTO (2021a), (n52) [89], [91]; WTO (2020), 11.

\textsuperscript{74} Industrial design protection—if at all to become a barrier to accessing essential health products used in the pandemic response—is more likely to limit the distribution and use of ventilators, PPE, and diagnostic tools such as rapid antigen tests (RATs) and polymerase chain reaction (PCR) tests, than inputs for vaccine production.
in force in a particular jurisdiction, or a NVUA is granted under a patent, access to confidential information and related know-how may still be necessary to ensure the effective implementation of the technology platform. Removing barriers and obtaining access to confidential information is therefore critical to technology transfer and generic vaccine production.

5.2.4 Clinical Trial Data

Clinical trial or test data demonstrating the safety and efficacy of new pharmaceuticals is, in some countries, required to be submitted to regulatory authorities as a condition of approval for new products and applications. Such data may also include sensitive information regarding the manufacturing process, formulation, dosage, delivery method, indicated uses, and general safety information. These regulatory procedures are distinct from the protection of IP as such, and many countries do not maintain entirely independent approval processes that call for data submission. Many base domestic approval on approval in other countries or WHO emergency use or prequalification procedures, particularly in urgent pandemic responses.

However, under TRIPS Article 39.3, in countries where test data are required to be submitted, such data are required to be protected against disclosure or unfair commercial use (Taubman 2008b), provided they are undisclosed, relate to a new chemical entity, and require considerable effort to generate. This requirement may constrain firms from producing follow-on COVID-19 vaccines. The relevant TRIPS standards apply when the domestic authorities undertake a distinct review of clinical trial data as a condition of regulatory approval. Some bilateral and regional agreements provide for more extensive protection, which may expressly set a term of exclusivity over the originator’s data, apply to reliance on data submitted for approval in other jurisdictions, or set limits over reliance on the originator’s earlier regulatory approval. Reportedly, regulatory systems and processes in Asia and the Pacific have previously slowed or blocked the introduction of externally developed novel vaccines (Tsai, Rao, and Xu 2018). Because of relatively low costs and growing technical expertise, there has been an increasing trend in

75 WTO (2021d), (n 88) [35].
76 See, e.g., Comprehensive and Progressive Agreement for Trans-Pacific Partnership (signed 8 March 2018) incorporating the Trans-Pacific Partnership Agreement (signed 4 February 2016) art 18.50.
recent years for clinical trials to be conducted in the region (Ali et al. 2019), including for COVID-19 vaccines.

Countries in Asia and the Pacific maintain a diverse range of approaches to both regulatory approval of vaccines (including reliance on approval in other jurisdictions or by WHO), and the protection of clinical trial data. Divergent regulatory mechanisms and cumbersome regulatory procedures have been identified as an obstacle to the timely production and distribution of vaccines (OECD 2021).

Malaysia imposes a data exclusivity requirement, but this excludes situations where compulsory licenses have been issued and any other measures consistent with the need to protect public health. The provision clarifies that the government may take necessary action to protect public health, national security, noncommercial public use, national emergency, public health crisis, or other extremely urgent circumstances declared by the government.77

As Article 39.3 has no applicability where no test or other data are required to be submitted, other countries may continue omitting the requirement to submit test data as a condition for the market approval of pharmaceutical products. Cambodia, for example, does not impose requirements to submit such data as a condition for pharmaceuticals to be imported, produced, or exported under a compulsory license.78 In such cases, members may opt to permit their regulatory approval bodies to rely on foreign test data or regulatory approval, in which case no submission to the relevant authority is required (Spina Ali 2018). This may also be achieved through regional approval mechanisms or WHO prequalification and emergency listing procedures.

A key concern is the extent to which data exclusivity requirements may impede the use of compulsory licenses, including those issued to give effect to the Paragraph 6 System (Meitinger 2005). One proposal is to include a carve-out for compulsory licenses in those regimes where data exclusivity is enforced (‘t Hoen, Boulet, and Baker 2017). Malaysia incorporates this clarification into its law,79 as does Cambodia, whose law provides that “[t]he protection conferred to test data and other undisclosed information shall not be invoked to prevent, impede or delay the execution of a compulsory licence.”80

78 Cambodian Compulsory Licensing Law (n57) art 18.
79 Cambodian Compulsory Licensing Law (n102).
80 Cambodian Compulsory Licensing Law (n 20) art 17.
5.2.5 Restrictive Licensing and Anticompetitive Practices

Often overlooked among the tools available to members wishing to provide greater protection for public health, and in place of more IP-focused mechanisms (Anderson, Müller, and Taubman 2021), are measures aimed at addressing anticompetitive practices. These two regimes of IP protection and anti-competition are far from inherently inconsistent. They may function as two practical policy levers for achieving a balance of incentives and technology transfer promotion (Anderson, Taubman, and Carvalho 2021; Anderson 2003). Indeed, anticompetitive principles need not emerge solely as independent rules and provisions but may also contribute to the development of balanced domestic IP law. Competition law may play a remedial role, especially where an IP regime is seen as being ill-suited for addressing the peculiarities of a significant health crisis.

A common manifestation of anticompetitive practices in the IP context is restrictive voluntary licensing terms (Drexl 2005); TRIPS expressly recognizes anticompetitive practices as grounds for compulsory licensing.

India’s law includes the “reasonable requirements of public not being satisfied” as one ground for the issue of a compulsory license. It deems this to be the case where a patentee imposes one of the conditions listed in Article 42.2.81 Mongolia’s law provides cases where “the patent owner sets unacceptable terms for the exploitation of the invention” as a ground for compulsory licensing,82 while Viet Nam’s law provides cases where the patent holder “is considered [to have] performed anti-competition practices banned by competition law.”83

5.2.6 Remedies for Infringement

Laws on remedies for IP infringement can be crafted to manage abusive IP practices, for public interest purposes such as public health protection. The minimum TRIPS requirements for remedies are set out in Part III, Section 2. It follows that, even in cases other than the compulsory use of the patented subject matter, a member’s judicial authorities must merely “have the authority” to issue an injunction. Therefore, a member’s authorities need not award an injunction in all cases. The same is true with respect to ex post compensation or damages for “injury ... suffered

81 Indian Patent Law (n 20) s 84(7). See also Indian Patent Law s 84(1).
82 Mongolian Patent Law (n 20) art 20.
83 Vietnamese Intellectual Property Law (n 41) art 145(d).
because of an infringement,”84 which is distinct from the remuneration paid for IP use. In each case, public interest considerations may be weighed against the rights holder’s legitimate interests in determining the amount of remuneration and/or compensation to be paid (Médecins Sans Frontières 2015, 1). The reference to IP “infringement” suggests that no injunctive relief is required unless such infringement is established, thus ruling out interlocutory relief as a requirement and enabling vaccine production to continue in the public interest. Of course, interlocutory action for imminent or ongoing infringement is a legitimate means of preventing the unauthorized use of protected IP subject matter. Therefore, removing the availability of provisional relief may be reserved for IP subject matter that is essential to the pandemic response.

5.3 Legal and Policy Options

5.3.1 Strengthening the Factual Basis for Decisions on Intellectual Property Law and Policy

A. Short- and Longer-Term Approach to Sustained Access to Vaccines

In assessing options for short- and longer-term approaches to sustained access to vaccines, policymakers should consider whether a country or group of countries is likely to remain largely reliant on imported vaccines or has actual or potential production capacity. Equally, a significant consideration is whether a country has, or plans to develop, substantial capacity for vaccine R&D. An objective review of these questions would enable a more tailored, nuanced approach to integrating IP law and policy with innovation and access programs. This would be better suited to individual countries’ specific needs and circumstances while strengthening the basis for regional cooperation.

Members should therefore assess IP legal and policy frameworks based on immediate and longer-term options for vaccine access, develop IP management policies for publicly funded R&D, and strengthen planning and strategic partnerships with regional countries and institutions, with a view to collaborative access and development programs.

84 TRIPS art 45.
B. Illuminating the IP Landscape
Immediate and longer-term action will be better informed and more effective if it is based on a clearer understanding of the actual state of play concerning IP coverage, keeping in mind that the situation is likely to vary significantly within and across regions. This entails preparing landscape studies that would (i) illuminate the extent to which background and foreground IP, especially patents, have been protected in jurisdictions across the region; and (ii) consider whether, and to what extent, test data protection applies to regulatory approval outcomes in jurisdictions across the region.

A clearer mapping of the IP landscape may reveal that IP-related barriers to vaccine access in certain jurisdictions or regions are more hypothetical than real. However, there are considerable challenges in maintaining an up-to-date and accurate analysis of a fast-evolving and complex technology landscape.

Therefore, members should strengthen their analytical capacity and seek technical assistance in tracking patent and other registration activity, assessing the impact of clinical trial data protection, and map requirements for the submission of such data. They should also work with regional partners and institutions to develop a coordinated approach to technology tracking and IP mapping exercises.

5.3.2 Legal and Legislative Framework for the IP System
Despite the enormous challenges of the domestic and the international response to the pandemic, policymakers have a good opportunity to assess the adequacy and appropriate balance of IP laws for health innovation and access, given the hard lessons learned during this public health crisis. The review process may include considering whether:

- the criteria for grant of patents and other IP rights are well adapted to domestic and regional needs and circumstances, while conforming with the principles laid down in international agreements (e.g., TRIPS);
- suitable exceptions to patents and other IP rights, as discussed in Section 5.2.1.B, have been included in legislation, to ensure scope for precommercialization activities such as experimentation, research, and regulatory approval; and
- suitable, balanced rules and streamlined, clear procedures have been included in legislation providing for use in the public interest of patented subject matter without the right holder’s
consent either on the initiative of government authorities, or following the application of interested third parties.

To tackle this complex task, members can take two key steps in particular: (i) undertake a multi-stakeholder public health review of IP laws in terms of both overall settings and specific measures, to enhance innovation and access in a way tailored to domestic needs and priorities; and (ii) coordinate review process with regional partners and regional and international institutions, to promote synergies, mutual learning, and best practices.

Applications for IP rights are assessed, examined, granted, and administered under national systems of domestic law, rather than at the international level (except under regional mechanisms, where applicable). Hence, achieving a beneficial balance of rights and interests under the IP system in a practical sense is determined almost exclusively through domestic action, reinforced as needed by enhanced agency of domestic institutions. Hence, it is critical to guarantee the availability of the necessary technical capacity and human capital required for effective administration, as well as the essential resources to ensure greater transparency of granted IP rights and applications in process, and their compliance with domestic and international standards.

To ensure that these elements are in place, members may wish to clarify and streamline procedures for the timely grant of IP rights and the availability of opposition procedures and applications for compulsory licensing and other interventions, as well as integrate such procedures with international systems to facilitate and support administration and transparency. Increased transparency can be achieved through the timely publication of applications, decisions on grants, and grants of IP rights.

5.3.3 Coordinated and Collaborative Access Mechanisms

In the spirit of solidarity, the effective agency of national governments in leveraging immediate and sustainable access to vaccines and other medicines is enhanced in practice through regional coordination and cooperation. To achieve this, members must address multiple countries’ demand for vaccines to enhance leverage and create economies of scale by linking different forms of NVUAs and proceeding to pooled or coordinated procurement, and by using regional and international mechanisms to coordinate a cooperative approach.
5.4 Conclusion

So far, relatively little attention has been paid to how IP flexibilities in their current form might be more effectively and widely implemented to promote access to pandemic response products. When leveraged at the domestic level, such options present powerful tools for increasing local production of vaccines and other essential medicines and for improving their availability within developed nations. When utilized and deployed by groups of countries in cooperation, they open up avenues for reinforcing government agency, aggregating demand, creating economies of scale, and developing resistance against potential political and industrial pressure. Finding an appropriate balance of IP laws for health innovation and access in combination with a strong policy framework should significantly spur vaccine production and facilitate access to other health technologies in the pandemic context and for future public health crises.
References


Implementing Flexibilities of Trade-Related Aspects of Intellectual Property Rights to Spur Vaccine Production


Implementing Flexibilities of Trade-Related Aspects of Intellectual Property Rights to Spur Vaccine Production


PART II

Production, Trade and Transport of Vaccines
6

Analyzing Trade Barriers for Vaccines and Vaccine Inputs: Learnings from Asia and the Pacific

Pralok Gupta and Ayona Bhattacharjee

6.1 Introduction

The coronavirus disease (COVID-19) pandemic took the world by surprise, resulting in huge demand and supply shocks in different sectors, especially in the health-care sector. During the pandemic, production and availability of COVID-19 vaccines became most relevant as they provided hope for containing the pandemic. While the role of vaccines in prevention and control of outbreaks of infectious diseases is well established, not all countries are capable of producing them (OECD 2021). Limited domestic capacities combined with infrastructure and policy bottlenecks have often resulted in vaccine stockouts in many countries (WTO 2020). In several such cases, international trade has been instrumental in overcoming these challenges (OECD 2021). Despite immense potential for global expansion of vaccine markets and the World Trade Organization (WTO) reporting a fivefold increase in traditional vaccine trade since 2005, many regulatory hurdles remained, which affected their trade flows (WTO 2020). Regulatory restrictions combined with other forms of tariff and non-tariff measures (NTMs), purportedly aimed at protecting public health, affect the availability, accessibility, and affordability of vaccines and hence the immunization rates across countries. Accordingly, the mechanism linking trade and

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1 This chapter is significantly based on a previous version of this paper published in the Asia-Pacific Sustainable Development Journal (Vol. 29, No. 2, 2022).
vaccine availability remains an important aspect worth exploring (Helble and Shepherd 2017).

In this context, this chapter contributes to the literature through the analysis of trade flows, trade barriers, and trade policies related to vaccines and vaccine inputs in Asia and the Pacific. Selection of Asia and the Pacific for this study is attributed to the region’s rising trade share for vaccines and vaccine inputs over the past 2 decades, second only to the trade flows that Europe and Central Asia reported. In fact, the rise in export and import shares of vaccines and vaccine inputs have been higher in Asia and the Pacific than the corresponding increase reported globally during the 2000–2020 period. This chapter provides a broad analysis of trade trends and patterns of vaccines and related inputs in the region while identifying the major trading economies and their key trading partners. It analyzes tariff and non-tariff barriers on vaccines and related inputs that were imposed by economies in this region. It also provides a cross-country comparison of trade policy responses, including export restrictions for vaccines and vaccine inputs in response to COVID-19. To better understand the current and future trade-related issues concerning vaccines and related inputs, this study also includes findings from a survey of key stakeholders in India, a significant player for vaccines in the region.

6.2 Trade Trends and Patterns of Vaccines and Related Inputs

The WTO (2021a) published the Joint Indicative List of the critical inputs for the manufacture, distribution, and administration of COVID-19 vaccines (Table 6.1). To study vaccine inputs trade, the analysis is based on this list, as it is the only available comprehensive list for vaccine inputs. The list consists of 54 products under vaccine manufacturing (VM), eight under vaccine administration (VA), and four under vaccine storage and distribution (VSD), covering 66 critical inputs related to COVID-19 vaccines. The products listed under VM are further categorized into active ingredients, inactive ingredients, other ingredients, consumables, equipment, and products for packaging purposes.

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2 Authors’ calculations from the World Integrated Trade Solution (WITS).
3 The list was jointly produced by the Asian Development Bank (ADB), the Organisation for Economic Co-operation and Development (OECD), the World Customs Organization (WCO), some COVID-19 vaccine manufacturers, researchers Chad Bown and Chris Rogers, the Coalition for Epidemic Preparedness Innovations, and DHL.
The Harmonized System (HS) HS17–HS96 correspondence tables are used to identify the HS96 product codes so that their trade patterns can be analyzed for the 2000–2020 period. In the process, the active ingredients category, namely HS product code 300220, is separated out from the list of VM products as it represents vaccines (for human medicines). Subsequently, the trade-related trends, patterns, and policies for this product code are analyzed.

An analysis of trade data on vaccines (HS Code 300220) indicated that global exports of vaccines have steadily increased over time, though most trade shares were held by developed countries (footnote 1). The Asia and Pacific region remained a net importer of vaccines during 2000–2020, with rising imports over recent years. Most economies in the region were also net importers of vaccine inputs, except the People’s Republic of China (PRC), Japan, and Singapore, which were net exporters of VM inputs; the PRC, Indonesia, and the Republic of Korea (ROK) were net exporters of VA inputs; and the PRC, Malaysia, and the ROK were net exporters of VSD inputs. On the other hand, the PRC and Japan have been major importers of VM and VA inputs; and Japan and Hong Kong, China have held major shares for VSD inputs. Thus, within Asia and the Pacific during 2000–2020, some of the major trading economies for both vaccines and vaccine inputs have been the PRC, Indonesia, and the Republic of Korea.

### Table 6.1: Classification of Critical COVID-19 Vaccine Inputs

<table>
<thead>
<tr>
<th>Category</th>
<th>Subcategory</th>
<th>No. of Products Listed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine manufacturing (VM)</td>
<td>Active ingredients</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Inactive ingredients</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Other ingredients</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Consumables</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Equipment</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Packaging</td>
<td>3</td>
</tr>
<tr>
<td>Vaccine administration (VA)</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Vaccine storage and distribution (VSD)</td>
<td></td>
<td>4</td>
</tr>
</tbody>
</table>

COVID-19 = coronavirus disease.

Note: HS2017 classification is used for categorizing the products. The classification is based on a list of 83 products, six of which have HS2017 codes missing. Some products within the group of VM are repeated and one product, identified as an equipment in the VM category (Code 842230), does not have data. Thus, trade-related data are available for only 66 products. A detailed description for each product is provided in Table 6A.1 in the appendix.

Japan, and the ROK. The major traders of vaccines and vaccine inputs and their trading partners are reported in Table 6A.2 in the appendix.

The leading exporters and importers of vaccine manufacturing, storage and distribution, and administration inputs in Asia and the Pacific are represented in Figure 6.1. Within this region, economy-wise export shares of vaccine input groups have varied over time. While the share of the PRC in the exports of all vaccine input groups has increased significantly, the shares of Japan have declined significantly.

**Figure 6.1: Shares of Leading Exporters and Importers of Vaccine Inputs in Asia and the Pacific, 2000–2020 (%)**

- **A. Leading exporters, manufacturing inputs**
  - 2000: PRC, Singapore, Thailand, Japan, Korea, Rep. of
  - 2020: PRC, Japan, Korea, Rep. of

- **C. Leading exporters, storage and distribution inputs**
  - 2000: PRC, Turkey, Thailand, Korea, Rep. of
  - 2020: PRC, Turkey, Thailand, Korea, Rep. of

- **E. Leading exporters, administration inputs**
  - 2000: PRC, Japan, Malaysia, Thailand
  - 2020: PRC, Japan, Malaysia, Thailand

- **B. Leading importers, manufacturing inputs**
  - 2000: PRC, Korea, Rep. of, Japan, India
  - 2020: PRC, Korea, Rep. of, Japan, India

- **D. Leading importers, storage and distribution inputs**
  - 2000: PRC, Korea, Rep. of, Japan
  - 2020: PRC, Korea, Rep. of, Japan

- **F. Leading importers, administration inputs**
  - 2000: PRC, Korea, Rep. of, Japan
  - 2020: PRC, Korea, Rep. of, Japan

PRC = People’s Republic of China.

Source: Data are from the World Integrated Trade Solution (WITS) database.
It was also found that almost three-fourths of the VSD input imports were intraregional (Figure 6.2). Contrary to the intraregional sourcing of vaccine inputs, Asia and the Pacific economies have reported very high import dependence on the rest of the world for vaccines. These findings imply the potential for greater intraregional trade ties to facilitate trade in vaccine inputs and improve the availability of inputs for vaccine production in the region.

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**Figure 6.2: Import Dependence of Vaccine Input Groups and Vaccines of Asia and the Pacific from within the Region vs. the Rest of the World (%)**

- **A. Vaccines (Code 300220)**
- **B. Vaccine manufacturing inputs**
- **C. Vaccine administration inputs**
- **D. Vaccines storage and distribution inputs**

**Notes:** The data have been segregated based on trading partners being the world or Asia and the Pacific economies; trade with the rest of the world has been computed as the difference in total import (in trade values) between the world and economies in the region. The import shares have been computed as a percentage of total imports from either Asia and the Pacific or from the rest of the world, for each product category.

**Source:** Data extracted from the World Integrated Trade Solution (WITS) database.

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To infer the extent of import dependence of the individual economies within the region, the Herfindahl–Hirschman index (HHI) is calculated for their respective import of vaccines (Table 6A.3 in the appendix) and vaccine inputs (Table 6A.4 in the appendix). The indices show that only a few economies have exhibited concentrated sourcing of imports. While import concentration was higher in 2020 compared to that in
2015 for countries such as Brunei Darussalam, Georgia, and Myanmar, many others in the region reported lower import concentration in 2020. Some notable examples were Australia, Azerbaijan, Cambodia, Fiji, Kazakhstan, and Sri Lanka. Similar index calculation for vaccine inputs show that different economies exhibited different levels of diversification in their import dependence, depending on the type of vaccine inputs considered. While countries such as Mongolia reported concentrated import dependence, the PRC and Türkiye reported more diversified sources of imports. The HHI values in 2020 are greater than their values in 2015 for many of the selected economies, implying that the import concentration of vaccine inputs for these economies was higher in 2020 than in 2015.

6.3 Trade Policy Analyses for Vaccines and Vaccine Inputs in Asia and the Pacific

The analysis of trade policies (tariff and non-tariff barriers) and resultant bottlenecks for vaccines and vaccine inputs is important as the delay of a single input can significantly disrupt the process of vaccine production and hamper supply chains. This section contains a discussion of the trade policies pertaining to vaccines and their inputs in the region.

6.3.1 Analysis of Tariff Barriers

Data on bound tariff, effectively applied tariff, and most favored nation (MFN) applied tariff are extracted from the Comtrade and inverted Comtrade databases. Bound tariff is the maximum MFN tariff level for a given commodity line, as specifically committed by WTO member countries. However, bound tariffs are not necessarily the rate which the WTO member countries apply actually. In practice, the applied tariff is less than or equal to the bound tariff for any product. Wide differences between bound tariffs and applied MFN rates are visible across certain products in certain countries, making their trade policies less predictable. For example, India reported a bound tariff of 150% on product code 220720 (ethyl alcohol and other spirit) in 2020, but the applied MFN rate for this product code for the same year was 30% only.

The highest effectively applied tariff rates imposed by any country in the region on vaccines during 2015–2020 were those of India at 10%

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4 WITS uses the concept of effectively applied tariff, which is defined as the lowest available tariff. If a preferential tariff exists, it is used as the effectively applied tariff. Otherwise, the MFN applied tariff is used. Thus, effectively applied tariff is equal to the MFN applied tariff unless a preferential tariff exists (World Bank 2011).
in 2015, which declined to approximately 8% the following year. In Asia and the Pacific, the effectively applied tariffs have remained relatively high in only a few economies, such as India, Pakistan, and French Polynesia. On the other hand, countries such as Australia, Singapore, and Viet Nam, among others, kept vaccines duty-free during this period. It is worth mentioning that the tariffs imposed on vaccines have usually been much lower than those imposed on vaccine inputs.

Figure 6.3 shows that most economies in Asia and the Pacific imposed very low tariffs on vaccines. Compared to the conditions prevailing in 2015, a smaller share of countries reported MFN tariffs greater than 10% in 2020, and a larger share reported tariffs between 2.5% and 5%. From 2015 to 2020, MFN tariff rates were reduced in some economies, including Pakistan (from 6.7% to 3.7%), Kazakhstan (from 2.9% to 0%), and the Russian Federation (from 2.9% to 2%), whereas others increased their MFN tariffs on vaccines during this period, such as the PRC (from 0% to 3%), Palau (from 0% to 3%), Armenia (from 0% to 2%), and the Kyrgyz Republic (from 0.7% to 2%).

A cross-economy comparison of the effectively applied tariffs on vaccine imports shows that within Asia and the Pacific, India, the Islamic Republic of Iran, Mongolia, Pakistan, and French Polynesia have
been the most restrictive, while most other economies in the region have not applied any tariff (Table 6A.5 in the appendix).

To identify and analyze trade barriers arising due to tariffs on vaccine inputs, economy-level data were extracted on effectively applied tariffs, considering the rest of the world as the trading partner. In addition, the researchers also extracted data on bound and MFN applied tariffs. Cross-economy simple averages of effectively applied tariffs for each vaccine input group are presented in Figure 6.4. As is evident, during 2015–2020, the lowest range of applied tariffs was reported on VM inputs, with slight reductions since 2018. VA or VSD inputs had relatively higher rates of applied tariffs during the same period. While the average applied tariff on VA inputs declined since 2018, the applied rates on VSD inputs have increased, especially since 2017.

In Asia and the Pacific, Indonesia imposed the highest simple average of the effectively applied tariffs on VM inputs in 2017. During 2015–2020, the average effectively applied tariffs were high in Maldives, Afghanistan, and India, whereas Brunei Darussalam, Georgia, and New Zealand maintained relatively low levels of effectively applied tariffs.

The analysis is based on economies reporting a minimum number of observations on tariff data.
Singapore; Hong Kong, China; and Macau, China have remained duty-free for VM inputs during this period.

Figure 6.5 shows the share of countries reporting high versus low tariffs, as of 2015 and 2020. Panel (A) shows that a fewer proportion of countries reported MFN tariffs greater than 10% in 2020 and a larger proportion of countries reported MFN tariff rates between 2.5% and

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**Figure 6.5: Most Favored Nation Applied Tariffs on Vaccine Inputs, by Duty Range, 2015 and 2020 (% of reporting economies)**

**A. Vaccine manufacturing inputs**

<table>
<thead>
<tr>
<th>Duty Range</th>
<th>2015</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 &lt; -2.5</td>
<td>0.20</td>
<td>0.16</td>
</tr>
<tr>
<td>2.5 &lt; -5</td>
<td>0.40</td>
<td>0.23</td>
</tr>
<tr>
<td>5 &lt; -10</td>
<td>0.20</td>
<td>0.29</td>
</tr>
<tr>
<td>&gt; 10</td>
<td>0.02</td>
<td>0.04</td>
</tr>
</tbody>
</table>

**B. Vaccine administration inputs**

<table>
<thead>
<tr>
<th>Duty Range</th>
<th>2015</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 &lt; -2.5</td>
<td>0.38</td>
<td>0.30</td>
</tr>
<tr>
<td>2.5 &lt; -5</td>
<td>0.18</td>
<td>0.23</td>
</tr>
<tr>
<td>5 &lt; -10</td>
<td>0.31</td>
<td>0.14</td>
</tr>
<tr>
<td>&gt; 10</td>
<td>0.17</td>
<td>0.34</td>
</tr>
</tbody>
</table>

**C. Vaccine storage and distribution inputs**

<table>
<thead>
<tr>
<th>Duty Range</th>
<th>2015</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 &lt; -2.5</td>
<td>0.51</td>
<td>0.19</td>
</tr>
<tr>
<td>2.5 &lt; -5</td>
<td>0.11</td>
<td>0.13</td>
</tr>
<tr>
<td>5 &lt; -10</td>
<td>0.17</td>
<td>0.35</td>
</tr>
<tr>
<td>&gt; 10</td>
<td>0.20</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Note: The pie charts represent the percentage of Asia and the Pacific economies reporting most favored nation (MFN) tariffs as per the tariff bands mentioned. Two years, 2015 and 2020, corresponding to pre- and post-pandemic times, are selected for comparing the share of economies reporting tariffs as per different tariff bands.

Source: Data extracted from the World Integrated Trade Solution (WITS) database corresponding to economy-level MFN applied rates imposed on vaccine inputs during 2015–2020.
5% in 2020. Panel (B) shows that fewer countries reported MFN tariffs greater than 10% in 2020, while more countries reported lower MFN tariff rates compared to those in 2015 for VA inputs. The change in the share of countries reporting low tariffs signifies a reduction in trade restrictiveness across the region. Panel (C) shows that far fewer countries reported MFN tariffs greater than 10% in 2020, while a larger share of countries reported MFN tariffs less than 2.5% or between 5% and 10% compared to those reporting in 2015.

Across the sample covering Asia and the Pacific during 2015–2020, the highest effectively applied tariffs were imposed on inactive ingredients, ethanol, chemically pure sucrose, or consumables (e.g., liquid storage bags of polymers of ethylene and plastics), while the lowest tariffs were imposed on equipment (e.g., chromatography systems) or ingredients (e.g., potassium chloride in bulk, neomycin, and cholesterol). Australia, the Lao People’s Democratic Republic, and Türkiye have maintained low average rates of effectively applied tariffs. Brunei Darussalam; Georgia; Hong Kong, China; Macau, China; Malaysia; New Zealand; and Singapore remained duty-free for VA inputs during this period.

### 6.3.2 Tariff Reduction or Elimination on Vaccines after COVID-19

Some economies reduced or eliminated tariffs on vaccines in response to the COVID-19 pandemic to reduce the cost of vaccines and enhance the supply. Among various policy instruments used during 2020–2021, 62.6% were in the form of tariffs, followed by non-automatic licensing, quotas (Global Trade Alert webpage). Detailed information on countries reducing tariffs on vaccines is scanty and differs across various databases.

Recognizing the need for cooperation to fight the pandemic, WTO members, including several in Asia and the Pacific, agreed to regularly review and eliminate unnecessary existing restrictions on exports of essential medical goods, refrain from imposing export restrictions, export taxes, remove or reduce tariffs which were considered important for vaccines, among other measures (WTO webpage on COVID-19 proposals). Many economies in Asia and the Pacific even agreed to enter into urgent consultations with any other affected member in case the measures disrupt supply chains and affect that member’s access to essential medical goods. They even agreed to accelerate the implementation of the Trade Facilitation Agreement provisions that support the timely and efficient release of goods (WTO 2021c).

Table 6.2 provides examples of some countries in Asia and the Pacific where tariffs on vaccines were reduced, in some cases temporarily, in response to COVID-19.
Table 6.2: Tariff Reduction on Vaccines in Asia and the Pacific after COVID-19

<table>
<thead>
<tr>
<th>Country</th>
<th>Measure</th>
<th>Countries Affected</th>
<th>Start Date</th>
<th>End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiji</td>
<td>Temporary elimination of value-added tax on imports of certain products, such as vaccines and pharmaceutical products, due to the COVID-19 pandemic.</td>
<td>All countries</td>
<td>26 March 2020</td>
<td>Unknown</td>
</tr>
<tr>
<td>India</td>
<td>Import duty waived on COVID-19 drug remdesivir, vaccines, oxygen, and related gear.</td>
<td>All countries</td>
<td>20 April 2021</td>
<td>31 October 2021</td>
</tr>
<tr>
<td>India</td>
<td>Certain domestic requirements regarding exports of vaccines were announced.</td>
<td>All countries</td>
<td>25 March 2021</td>
<td>Unknown</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Imports of COVID-19 vaccines are exempted from import tariffs and value-added tax.</td>
<td>All countries</td>
<td>26 November 2020</td>
<td>Unknown</td>
</tr>
<tr>
<td>Philippines</td>
<td>Tax-free and duty-free importation of COVID-19 vaccines.</td>
<td>All countries</td>
<td>26 December 2020</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

COVID-19 = coronavirus disease.

Sources: Based on International Trade Centre Market Access Map, United Nations Conference on Trade and Development, and World Trade Organization databases.

6.3.3 Analysis of Non-tariff Measures

Non-tariff measures play an important role in global trade of medical goods, including vaccines. Many countries have often used these measures during the COVID-19 pandemic to meet different trade and non-trade objectives. For instance, NTMs, such as export restrictions, have been used to prevent shortages of supplies of medical products in exporting countries as a reaction to increased domestic demand, whereas other NTMs have been adapted to facilitate imports of important goods (UNCTAD 2021). Accordingly, it is relevant to analyze the prevalence of NTMs on vaccine and vaccine inputs trade. For this purpose, the NTM nomenclature for this study is based on the revised classification of NTMs (UNCTAD 2019), which includes, for example, sanitary and phytosanitary (SPS) and technical barriers to trade (TBT), import licensing, prohibitions, quantity control measures, price control measures, and export-related measures (Table 6.3).
## Table 6.3: Trade-Facilitating and Trade-Restricting Non-tariff Measures

<table>
<thead>
<tr>
<th>Trade Facilitating Measures</th>
<th>Trade-Restricting Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>L41 Tax and duty exemptions, reductions, other fiscal incentives reducing burden of taxes otherwise due</td>
<td>P31 Export prohibition</td>
</tr>
<tr>
<td>G4 Regulations concerning terms of payment for imports</td>
<td>P33 Licensing, permit or registration requirements to export</td>
</tr>
<tr>
<td>E125 Licensing for the protection of public health</td>
<td>A11 Prohibitions for SPS reasons</td>
</tr>
<tr>
<td>A83 Certification requirements for SPS reasons</td>
<td>E313 Temporary prohibition, including suspension of issuance of licenses</td>
</tr>
<tr>
<td>L11 Transfers of funds (monetary transfers) by the Government (to an enterprise) – Grants</td>
<td>P32 Export quotas</td>
</tr>
<tr>
<td>D12 Anti-dumping duties</td>
<td>P22 Export monitoring and surveillance requirements</td>
</tr>
<tr>
<td>B83 Certification requirements for TBT reasons</td>
<td>E325 Prohibition for the protection of public health</td>
</tr>
<tr>
<td>L9 Support for consumers or producers not elsewhere specified</td>
<td>C9 Other pre-shipment inspection formalities not elsewhere specified</td>
</tr>
<tr>
<td>E325 Prohibition for the protection of public health</td>
<td>B14 Authorization requirements for importing certain products TBT reasons</td>
</tr>
<tr>
<td>B7 Product quality, safety, or performance requirements for TBT reasons</td>
<td></td>
</tr>
<tr>
<td>B14 Authorization requirements for importing certain products TBT reasons</td>
<td></td>
</tr>
</tbody>
</table>

SPS = sanitary and phytosanitary, TBT = technical barriers to trade.


As per the United Nations Conference on Trade and Development (UNCTAD) data on NTMs, frequently used trade-restricting NTMs across the globe during the COVID-19 pandemic include export prohibitions, license or permit requirements to export, and import prohibitions for SPS reasons. Conversely, frequently used trade-facilitating NTMs include tax and duty exemptions, reductions, other fiscal incentives, relaxation of regulations concerning terms of payment for imports, and relaxation of licensing requirements. As far as NTMs for COVID-19 vaccines and vaccine inputs trade are concerned,
information is limited. This may be due to non-reporting of such NTMs by the imposing countries. UNCTAD provides very broad information on such NTMs based on the income group classification of developing and developed countries (Figure 6.6).

Figure 6.6: Non-tariff Measures on COVID-19 Vaccines

COVID-19 = coronavirus disease.


A search of non-tariff measure-related information was also conducted from the UNCTAD NTM database, the World Integrated Trade Solution (WITS) TRAINS database, the WTO database, and the International Trade Centre Market Access Map. Limited information is available pertaining to NTMs on COVID-19 vaccines in the context of Asia and the Pacific (Table 6.4).
From Lab to Jab: Improving Asia and the Pacific’s Readiness to Produce and Deliver Vaccines

Table 6.4: Non-tariff Measures on COVID-19 Vaccines in Asia and the Pacific

<table>
<thead>
<tr>
<th>Enacting Country</th>
<th>Measure Description</th>
<th>Measure Type</th>
<th>Effect on Trade</th>
</tr>
</thead>
<tbody>
<tr>
<td>China, People’s Rep. of</td>
<td>Announcement by the Ministry of Commerce, the Ministry of Industry and Information Technology, the National Health Commission, and the National Medical Products Administration (NMPA) on publication of the list of COVID-19 vaccines for exportation. To ensure the smooth exportation of COVID-19 vaccines and support international cooperation to fight the epidemic, the vaccines approved or conditionally approved by the NMPA are included in the “List of COVID-19 Vaccines for Exportation” (developed and manufactured by PRC enterprises). The list will be dynamically adjusted in due course according to NMPA marketing authorizations.</td>
<td>Export authorization of vaccines</td>
<td>Facilitating</td>
</tr>
<tr>
<td>Fiji</td>
<td>Temporary elimination of value-added tax (VAT) on imports of certain products, such as vaccines and pharmaceutical products (HS chapter 30); medical equipment (HS chapter 90); scanners and cameras used in medical examinations; hand sanitizers, and antibacterial hand wash; gloves, masks; disposable hair nets; disinfectant wipes; tissue papers; face shields (medical use); medical goggles and spectacles; protective garments of rubberized materials; long-sleeved medical gowns; ethanol for companies involved in hand sanitizer production; disinfectants/sterilization products; hospital beds; hydrogen peroxide; paper bed-sheets; thermometers; air purifiers; and boots (specifically used in the medical environment) due to the COVID-19 pandemic.</td>
<td>Tax and duty exemptions, reductions, other fiscal incentives reducing burden of taxes otherwise due</td>
<td>Facilitating</td>
</tr>
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</table>

continued on next page
### Table 6.4 continued

<table>
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<th>Measure Description</th>
<th>Measure Type</th>
<th>Effect on Trade</th>
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</thead>
<tbody>
<tr>
<td>India</td>
<td>Temporary elimination of import tariffs on certain goods to fight COVID-19, e.g., COVID-19 vaccines, oxygen concentrator, medical oxygen, oxygen canisters, oxygen filling systems, oxygen storage tanks, oxygen generator, ISO containers for shipping oxygen, oxygen cylinders including cryogenic cylinders and tanks, and ventilators.</td>
<td>Tax and duty exemptions, reductions, other fiscal incentives reducing burden of taxes otherwise due</td>
<td>Facilitating</td>
</tr>
<tr>
<td>India</td>
<td>Exemption of the Integrated Good and Services Taxes (IGST) on imports of COVID-19 relief goods, including vaccines.</td>
<td>Tax and duty exemptions, reductions, other fiscal incentives reducing burden of taxes otherwise due</td>
<td>Facilitating</td>
</tr>
<tr>
<td>India</td>
<td>Amendments introduced to the export policy of syringes with or without needles. The export policy is revised from “Free” to “Restricted” on 4 October 2021.</td>
<td>Export authorization of vaccine administration inputs</td>
<td>Restricting</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Exemption from import tariffs and VAT on COVID-19 vaccines.</td>
<td>Tax and duty exemptions, reductions, other fiscal incentives reducing burden of taxes otherwise due</td>
<td>Facilitating</td>
</tr>
<tr>
<td>Philippines</td>
<td>Tax-free and duty-free importation of COVID-19 vaccines.</td>
<td>Tax and duty exemptions, reductions, other fiscal incentives reducing burden of taxes otherwise due</td>
<td>Facilitating</td>
</tr>
</tbody>
</table>


Based on the analysis of the available information on NTMs, two interesting findings should be highlighted. First, some countries have imposed trade-facilitating NTMs on vaccines after the COVID-19 pandemic. However, many of the trade-restricting NTMs that were imposed prior to COVID-19 still exist. Second, these trade-restricting NTMs are not vaccine specific, but rather are imposed by such countries across many pharmaceutical products. For instance, Brunei Darussalam imposed import licensing requirements under its Poison Act in 2001 on various products, which also included some of the vaccine codes at the HS 8-digit level. Similarly in Pakistan, the Control of Narcotic Substances Act XXV of 1997 states that no one shall import, export, transport, or transship any narcotic drug. The HS codes included in the list of this act also include vaccine HS code 300220.

Many countries have resorted to export restrictions on vaccines, particularly after a surge in COVID-19 cases of the Delta variant. Section 3.4 provides a discussion on export restrictions on COVID-19 vaccines in selected economies in Asia and the Pacific.

### 6.3.4 Export Restrictions Imposed for Vaccines and Vaccine Inputs

In Asia and the Pacific, the leading exporter countries of vaccines and vaccine inputs are India, Japan, Malaysia, the PRC, the ROK, Thailand, Singapore, and Türkiye. The PRC is one of the world’s top exporters of COVID-19 vaccines. According to Bloomberg Businessweek (2021), the PRC has exported more than 1.5 billion doses of COVID-19 vaccines across the globe, and Sinovac Biotech Ltd. is the leading provider globally, having shipped 1.9 billion doses at home and overseas as of late September 2021. Similarly, India is reported to be a major exporter of the AstraZeneca vaccine to South Asia and rest of the world. More than 70 countries have received vaccines made in India.

Vaccine exports have been restricted in many countries, particularly after a surge in Delta variant cases. For instance, restrictions in India on the vaccine’s exports were enacted in response to domestic demand and the need to vaccinate the population after a significant rise in COVID-19 cases in April 2021. Vaccine exports from India resumed in November 2021. According to a WTO (2021c) report, at least 13 WTO members maintained measures that may affect the export of certain inputs included those on the Joint Indicative List of Critical COVID-19 Vaccine Inputs, as well as some active ingredients that are classified in the HS together with final vaccines (HS code 300220). Export restrictions continue to impede access to vaccine inputs and thus create uncertainty in vaccine supply chains. Restrictions persist on exports by vaccine manufacturers.
to foreign fill-and-finish sites, both for sites owned by the manufacturer and the contract development and manufacturing organizations that partner with vaccine manufacturers. In response to export restrictions, some countries have enacted measures to require local supplies of inputs, which has added bottlenecks to regulatory approval, added complexity to distribution planning, and further restricted vaccine availability in countries without extensive manufacturing infrastructure (WTO 2021c).

A large share of the billions of COVID-19 vaccines administered so far have been in high- and upper middle-income countries. These vaccines have not reached a large part of the world’s poorest people, including in Asia and the Pacific. Given the production capacity, vaccine exporters of Asia and the Pacific can play a significant role in increasing the supply of vaccines not only to this region but to the other parts of the world—and this can help to reduce the imbalance in the availability of vaccines across countries.

Apart from export restrictions on vaccines, restrictions on vaccine-related inputs also affect vaccination targets despite vaccine availability. For instance, the availability of syringes could affect vaccine administration in various countries. The global supply of syringes was hampered after a “quantitative restriction” was enacted in India on the export of certain categories of syringes for 3 months in October 2021. India placed these restrictions to boost the COVID-19 vaccination drive within the country. With India’s export restrictions on syringes in place from October to December 2021, the potential shortfall in 2022 is 2 billion to 4 billion needles in the global supply. The World Health Organization and the United Nations Children’s Fund (UNICEF) warned that the syringe shortage could have dire consequences for the global vaccination effort (New York Times 2021).

### 6.4 Survey Findings

To gain insights on trade-related issues concerning vaccines and related inputs, a survey of relevant stakeholders was conducted in India. Being a significant player for vaccines in Asia and the Pacific, India can provide substantial insights and takeaways for other trading countries. In this context, online personal interviews of 10 key stakeholders were conducted from December 2021 to February 2022 to better understand how regulatory frameworks, tariff and non-tariff barriers, constraints to production, scaling up, and vaccine nationalism can affect vaccine availability and its distribution, thereby providing lessons for future pandemics. The stakeholders contacted included representatives from pharmaceutical companies, subject experts, think tanks, and academics.
The main findings from the primary survey can be categorized into four broad pillars.6

6.4.1 Regulatory Framework for Vaccine Production and Trade-Related Barriers

Vaccines are public goods, but the global supply and trade in vaccines are subject to license-based regulatory frameworks. Trade is considered instrumental in facilitating access to and supply of goods. The same should hold true for vaccines or related inputs. However, as the pricing and purchase arrangements for vaccines have been dominated by high-income countries and selected pharmaceutical companies, smooth trade flows of vaccines were affected, especially for COVID-19 vaccines.

While tariffs are not considered critical for COVID-19 vaccines, NTMs have played a crucial role. Most of these NTMs are imposed by exporting countries, not importing countries. The most significant issue in the case of NTMs is the sharing of trade secrets and the control of technology. Licensing agreements can be obtained only for fill and finish but not for vaccine manufacturing. Contract manufacturing licensing exists, which implies that the contracted company is producing only for the contracting company and other countries cannot use it.

Harmonization of regulatory approval requirements has broadly been acceptable, but the level at which this should happen has remained an important issue for consideration. Global manufacturers do not support harmonization at a lower threshold, but if harmonization is aimed at higher levels, the compliance requirements for manufacturers from developing countries would increase.

The experience of India regarding Covaxin regulatory approval from WHO brings out issues related to appropriate rigorous documentation and data sharing. This may hold true for vaccine manufacturers of developing countries if they lack proper documentation for regulatory approvals. It affects the global benchmarking of their vaccines through WHO approval, in the absence of which they may not be able to supply it to other countries.

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6 It may be noted that the findings in this section represent the views of the respondents and not of the authors.
6.4.2 Vaccine Production and Scaling Up

Though India had a delayed start, it rapidly improved its vaccine rollout program. Government policies concerning, for example, boosters and vaccine rollouts have been playing an important role in the rollout of the vaccines. Vaccine manufacturing is a package that needs to be delivered to the targeted countries. Bulk manufacturing formulations can be transported to other countries provided the target country has a fill-and-finish facility and the capacity to do so. However, half of the developing countries do not have the required capacity. In such a situation, the option for enhancing supply in non-vaccine-producing countries is to transport ready-to-inject vaccines. Even post-production processes of vaccine distribution and administration is time consuming and requires pre-planning. This was probably a reason for the delayed rollout of vaccines in early 2020, leading to the widespread emergence of the Delta variant.

Inactivated virus vaccine platforms are relatively easier to handle. Large amounts of vaccines can be produced through such technologies. For example, Covaxin is produced using this technique. However, there are barriers associated with this method, such as the safety risks and the containment technologies required at a large scale. Many countries do not have such large containment technologies.

Global tendering of vaccines has not been a successful model of operation. The process of tendering vaccines may work differently for COVID-19 versus traditional vaccines. COVID-19 vaccines require rapidity, stringent storage requirements, robust supply chains, and high demand. Additionally, it is likely to be difficult to get suppliers through tendering in the middle of any pandemic. Bilateral agreements are likely to be more effective than global tendering for supplying vaccines and vaccine inputs across the countries.

6.4.3 Vaccine Nationalism

Vaccine nationalism has been evident during the COVID-19 pandemic. It is visible from a comparison of the number of doses supplied through the COVAX initiative and bilateral agreements such as Vaccine Maitri, compared with the number of vaccines administered in high-income countries. Vaccine nationalism in India was evident, but short-lived. It was solely due to the sudden emergence of the Delta wave in April 2021.
6.4.4 Lessons for Future Pandemics

Trade openness can be instrumental in the production of vaccines as one country alone cannot produce vaccines against all kinds of pathogens. Elimination of export and import barriers are important for vaccine trade, distribution, and administration. Input availability is a crucial determinant of vaccine availability. In some cases, these inputs are produced under trade secrets. In such cases, compulsory licensing can be issued.

A key takeaway from the pandemic is the need for higher investments in research and development and technology development related to vaccine production in Asia and the Pacific as well as globally. Another significant lesson from the production and trade of COVID-19 vaccines is the associated regulatory approval process. The usually long periods needed for approval were reduced to a 1-year window, implying that some of the commonly held assumptions of regulatory approval for already approved vaccines may have to be revisited.

6.5 Concluding Thoughts and Policy Recommendations

Most countries in Asia and the Pacific are import-dependent on vaccines and vaccine inputs. As the supply chains of all products can be adversely affected during a pandemic, as was evident with COVID-19, increased import concentration of countries may result in higher risks for the availability of vaccines or related inputs. Accordingly, countries need to diversify their sources of imports for vaccines and vaccine inputs.

The tariff analysis shows prevalence of high tariffs in some of the economies in Asia and the Pacific. Only a few of these economies had reduced or eliminated tariffs on vaccines during the COVID-19 pandemic. Economies need to bring down tariffs to decrease the cost of imports of vaccines and vaccine inputs. The analysis of NTMs shows a continuation of many of the NTMs that were imposed on vaccines prior to the COVID-19 pandemic. Most of these NTMs were not specific to vaccines but were imposed on vaccines together with other medical products. These legacy NTMs have the potential to delay the sourcing of vaccines and vaccine inputs from other countries. Therefore, these NTMs need to be identified by respective countries and eliminated if not of any particular significance.

There is a lack of transparency with respect to the administration of NTMs for vaccines and vaccine inputs trade and changes in these NTMs with the onslaught of the COVID-19 pandemic. Export restrictions have
significantly hampered the availability of COVID-19 vaccines in many countries. However, only a few selected countries had notified WTO of such NTMs and changes to them. It might be helpful if countries notify the applicable NTMs on vaccines and related inputs so that the manufacturers and exporters and importers of vaccines remain aware of them beforehand, as it would assist them in planning their inventories and minimizing any delay owing to the administration of such NTMs.

The PRC and India, being the two major global producers of vaccines in Asia and the Pacific, can play a significant role in enhancing intraregional trade in vaccines within the region. However, such potential may not be fully realized because of regulatory requirements from either the exporting country or the importing country or both sides. Regulatory coherence is required to enhance intraregional trade. Free trade agreements between or among countries in Asia and the Pacific may be used to ease import and export restrictions on vaccines and vaccine inputs. Such agreements need to have specific provisions for enhancing vaccine trade among the contracting parties.

Intraregional trade in Asia and the Pacific could also be increased by creating a regional hub for vaccines in the region. This requires regional cooperation for vaccines trade, which could be facilitated through the Economic and Social Commission for Asia and the Pacific. The institution can work toward using the strength and capabilities of producers of vaccines and related inputs in the region for creating such a regional hub for vaccines. The sharing of knowledge and harmonization of intraregional trade through this regional hub would help to enhance the distribution and administration of vaccines across countries in this region in normal times as well as during future pandemics.

Successful vaccine campaigns require not only adequate supply of vaccines but also logistic, storage, and distribution capacities. Accordingly, apart from ensuring adequate supply of vaccines through trade, equal emphasis should also be given to developing transportation and storage capabilities. While domestic demand is a key determinant of putting in place trade restrictions, the leading producers of vaccines should strive for the equitable distribution and availability of vaccines across countries as no one is safe until everyone is safe from infectious diseases such as COVID-19.


References


Appendix

Economies selected for this study:

Afghanistan; American Samoa; Armenia; Australia; Azerbaijan; Bangladesh; Bhutan; Brunei Darussalam; Cambodia; China (People’s Republic of); Cook Islands; Fiji; French Polynesia; Georgia; Guam; Hong Kong, China; India; Indonesia; Iran (Islamic Republic of); Japan; Kazakhstan; Kiribati; Korea (Republic of); Kyrgyz Republic; Lao People’s Democratic Republic; Macau, China; Malaysia; Maldives; Marshall Islands; Micronesia (Federated States of); Mongolia; Myanmar; Nauru; Nepal; New Caledonia; New Zealand; Niue; Northern Mariana Islands (Commonwealth of the); Pakistan; Palau; Papua New Guinea; Philippines; Russian Federation; Samoa; Singapore; Solomon Islands; Sri Lanka; Taipei, China; Tajikistan; Thailand; Timor-Leste; Tonga; Türkiye; Turkmenistan; Tuvalu; Uzbekistan; Vanuatu; Viet Nam

Note: Data for some of the economies for some years are missing. For the analysis, the maximum number of observations available is used.

Table 6A.1: Product Codes and Descriptions for Vaccine Input Groups

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HS = Harmonized System.

Table 6A.2: Vaccine Trading Partners of Leading Exporters and Importers of Vaccine Trade in Asia and the Pacific

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<tr>
<td>Viet Nam</td>
<td>Germany</td>
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PRC = People’s Republic of China.

Notes: The leading exporters and importers were identified on the basis of highest trade values of vaccine trade as reported by the economy. The major trading partners were identified from the descending order of percentage of import or export shares of vaccine trade for each economy and only five such partners have been reported.

Table 6A.3: Herfindahl–Hirschman Index of Import Dependence of Asia and the Pacific for Vaccines (HS Code 300220)

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<td>Viet Nam</td>
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</table>

HS = Harmonized System, N/A = data not available.

Notes: An increase in the index values is reported by some economies, such as Brunei Darussalam; Hong Kong, China; Malaysia; New Zealand; the Philippines; and Singapore.

### Table 6A.4: Herfindahl–Hirschman Index of Import Dependence of Asia and the Pacific for Vaccine Input Groups

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N/A = data not available, VA = vaccine administration, VM = vaccine manufacturing, VSD = vaccine storage and distribution.

Note: Most economies reported higher concentrated import dependencies in 2020 than in 2015. Kiribati is the only economy with smaller import concentrations in 2020 than in 2015, for all the vaccine input groups.

<table>
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<th>Economy</th>
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<th>Effectively Applied Tariffs on VA Inputs</th>
<th>Effectively Applied Tariffs on VSD Inputs</th>
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VA = vaccine administration, VM = vaccine manufacturing, VSD = vaccine storage and distribution.

Note: Simple average of the tariffs for each economy’s vaccine input combination was computed for 2000–2020.
7

Preparing for the Next Pandemic: Vaccine Global Value Chains and Local Production Capacity

Pavida Pananond and Alvaro Cuervo-Cazurra

7.1 Introduction

The coronavirus disease (COVID-19) pandemic has highlighted the crucial role of vaccines in public health management and economic development. The race for development, production, and distribution of COVID-19 vaccines has spotlighted how different countries take part in the vaccine global value chain. Because vaccine production is a complex process that involves different types of companies, a better understanding of how firms in different countries take part in the global value chains is instrumental in public policy planning regarding the promotion of local vaccine production. Building on the experience of COVID-19 vaccines, we analyze the preparedness and regional capacity of countries in the global supply chains of vaccines.

This chapter explains the rise of COVID-19 vaccine production and differentiates two approaches: internalization-driven production, whereby the leading pharmaceutical multinational corporations control most of the vaccine production in a few locations; and externalization-driven production, whereby lead companies extend their vaccine production to various regions. These two approaches are

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1 This chapter is an abridged version of a report commissioned by the United Nations Economic and Social Commission for Asia and the Pacific (ESCAP) and the World Health Organization. We thank suggestions for improvement from Witada Anukoonwattaka, Rupa Chanda, Pralok Gupta, Matthias Helble, Yern Fai Lee, and participants at the ESCAP conference on vaccine in Asia Pacific.
driven by multiple factors, including vaccine technology, strategy and missions of the vaccine producers, and the availability and capacity of qualified contract manufacturers. Reflecting on the experience with the development and distribution of COVID-19 vaccines helps better understand how countries can prepare for the next pandemic and how relevant parties and authorities can design appropriate policies for this purpose. We discuss the experience of Asia and the Pacific because countries in the region have diverse levels of capacity in vaccine manufacturing that illustrate the variety of potential alternative approaches.

The main message of this chapter is that the objective of governments during pandemics should be to achieve the necessary inoculation of the population in the most effective and rapid manner, not national production, even if the latter is a desirable goal for politicians. Preparing for the next pandemic can be done through a variety of means, of which local production is just one. Vaccine production comprises a chain of technologically advanced steps, each requiring high technological capacity and skilled personnel. A country’s readiness for vaccine production depends on an interaction of factors at the firm, value chain, and country levels. Countries with sufficient technological capability can focus on production participation. Countries with limited technological capacity need instead to focus on ensuring speedy access to vaccines produced elsewhere and effective and equitable access to distribution. Countries with higher technological capacity can encourage collaboration and participation in vaccine value chains for local production. The more complex the stage of vaccine production, the higher the need for technological capacity. Taking part in vaccine production should not be considered as an alternative to ensuring the efficient and fair distribution of vaccines.

7.2 The Global Vaccine Industry
Value Chain Characteristics

Two of the most important characteristics of the vaccine global value chain are the concentrated nature of vaccine production and the increased geographical segmentation of vaccine global value chains. Vaccine production is concentrated not only among a few pharmaceutical multinational companies but also in a few geographical locations in the world.

The vaccine industry has become increasingly concentrated among a few producers. For example, the number of companies producing vaccines for the market in the United States (US) decreased from more than 25 in the late 1970s to five firms 3 decades later (Institute of Medicine
Globally, four manufacturers—GlaxoSmithKline, Pfizer, Merck, and Sanofi—control 90% of global vaccine value. Similarly, more than 60% of global vaccine volume is produced by five leading firms—the Serum Institute of India (SII), GlaxoSmithKline, Sanofi, Bharat Biotech International Limited, and Haffkine (WHO 2020).

Additionally, vaccine production has also become geographically concentrated. The 13 countries that are referred to as the “Vaccine Club” host most of the global vaccine ingredients’ production (Evenett et al. 2021). These countries are home not only to final vaccine producers but also producers of vaccine ingredients, and subsidiaries of companies in the vaccine value chain. However, demand growth in emerging countries, along with advances in immunology and biotechnology, has expanded the participation of manufacturers headquartered in emerging economies in global vaccine value chains (Smith, Lipsitch, and Almond 2011). Midsize manufacturers, mostly in Asia, are increasingly extending their portfolios to compete in regional and new vaccine markets, offering additional and often more affordable choices (WHO 2020). The People’s Republic of China (PRC) and India have joined the club of leading global vaccine producers, with SII becoming the world’s largest vaccine manufacturer by volume.

The concentrated nature of the industry can be attributed to three main reasons. First, the high costs of research and development and the uncertainty of success serve as entry barriers. Only a few large companies with strong research and financial capability can afford and are willing to take this risk. Second, the high capital investment necessitates global economies of scale, which further erodes the number of potential competitors (Sell 2020). Third, prior to the COVID-19 pandemic, the financial profitability of vaccines was not as attractive compared to that of other drugs. Unlike drugs that can be taken over long periods, sometimes for life, vaccines are usually taken in a limited number of doses a few times in an individual’s life, resulting in their lower financial profitability (Thomas 2001; Kremer and Snyder 2003). Thus, the global market value for vaccines is estimated to be $33 billion in 2019, representing a mere 2% of the overall pharmaceutical market (WHO 2020).

### 7.3 COVID-19 Vaccine Value Chains

Getting a new vaccine from the laboratory into people’s arms worldwide is challenging. Before COVID-19, the entire process had never been completed in less than 4 years and often took more than a decade (Bown and Bollyky 2022). That the World Health Organization (WHO) and other national regulatory authorities approved some COVID-19 vaccines
by December 2020, less than a year after public reports of SARS-CoV-2 emerged, was an anomaly in the pharmaceutical industry.

As of April 2022, WHO has approved 10 vaccines for emergency use. These vaccines use several distinct technological platforms in their production: mRNA (Moderna and Pfizer–BioNTech), adenovirus vector (Johnson & Johnson, Oxford–AstraZeneca), and inactivated virus (Sinopharm, Sinovac, and Bharat Biotech). Some of these vaccines are based on the same formulation but adopt different trade names when produced by different facilities to be distributed in diverse geographical areas. For example, AstraZeneca’s vaccines are produced under two names—Vaxzevria and Covishield, with the latter being produced by SII mainly for distribution in developing economies. Similarly, SII also partners with Novavax, a US-based biotechnology company, to use the same vaccine formulation under a different trade name locally as Covovax.

7.3.1 Vaccine Production and Governance

The entire process of getting a vaccine, from developing it to delivering shots to the public, can be divided into four major stages (Bown and Bollyky 2022): research and development, clinical trials, manufacturing, and distribution. The first involves the preclinical stage of research and development to identify ways to induce the human immune system to react to antigens the same way that it would to a virus. The next stage comprises multiple rounds of clinical trials, with a smaller group of people in earlier phases to larger ones in later trials.

The manufacturing stage of vaccines, which is the focus of this chapter, comes next with two major phases: creating the bulk antigen, which is also known as active ingredient production, bulk production, or primary manufacturing; and formulating it into a drug product, which is often referred to as fill-to-finish or secondary manufacturing (Kis et al. 2020). Bulk antigen production is the most cost-intensive and complex step in the production process. High capital investments are required as the creation of new production facilities includes building and maintaining hyper-clean rooms, acquiring specialized equipment such as bioreactors and filtration pumps, and employing skilled personnel able to handle the mass production lines of vaccines. The formulation and fill phase, or form/fill for short, is the process under which the purified antigen or drug substance undergoes formulation into a drug product. Formulation processes can include combining the purified antigen with adjuvants to enhance the immune response in the body, stabilizers to ensure that the product remains potent until it is administered, or preservatives to ensure sterility in case
of multidose vials (UNIDO-WHO 2017). Filling refers to the step in which the formulated vaccine or drug product is filled into vials, plastic tubes, ampoules, or syringes. This process may occur in a separate manufacturing facility that undertakes the fill and finish (cap the vials and then label and package), resulting in different names of form-and-fill, fill-and-finish, or fill-to-finish (Bown and Bollyky 2022). This phase of vaccine manufacturing requires specialized assembly line equipment and facilities under strict temperature and sterility controls. Finally, once the filled vials are inspected, they are then packaged to undergo final quality control testing before being distributed for delivery. Some vaccines are transported frozen and in concentrated form, requiring on-site dilution before being administered to the public.

The pharmaceutical industry employs a range of organizational strategies for vaccine manufacturing. On one extreme are vertically integrated companies or organizations that perform most of the five stages in their facilities. However, such a hierarchical governance structure has shifted toward a more fragmented structure in which independent companies may specialize in specific stages of vaccine production. This process enables pharmaceutical companies to maximize their production efficiency without bearing the costs of undertaking all the production stages. Through contract development and manufacturing organizations (CDMOs), pharmaceutical firms have been able to engage independent and specialized biotechnology companies or academic institutions to take part in different activities in the pharmaceutical industry (Bown and Bollyky 2022). For COVID-19 vaccines, the only two vaccine developers who exclusively adopt end-to-end production are Sinopharm, developed by the China National Pharmaceutical Group, and Sputnik V, made by Gamaleya National Center of Epidemiology and Microbiology of the Russian Federation. Most other vaccine makers fall somewhere in the middle, with clusters of CDMOs present at both ends of the spectrum.

7.3.2 COVID-19 Production Capacity and Geographical Distribution

The COVID-19 pandemic has transformed the global vaccine manufacturing landscape, with capacity increasing almost fourfold by the end of 2022. Before the pandemic, the vaccine production capacity averaged around 5 billion doses annually (Airfinity 2021, cited in Guzman et al. 2022). In 2021, manufacturers produced 12 billion COVID-19 vaccines (Guzman et al. 2022), and the projected capacity for 2022 is 18.7 billion doses for the base case and even a higher 20.9 billion doses for the high case (UNICEF COVID-19 Market Dashboard).
COVID-19 vaccine production has been led by a limited number of vaccine developers: Pfizer–BioNTech, Moderna, Oxford–AstraZeneca, Janssen, Novavax, Bharat Biotech, Sinovac, and Sinopharm. Two other vaccines that are produced by India’s SII but are developed by others are Covishield and Covovax, which are developed by Oxford–AstraZeneca and Novavax, respectively. This chapter analyzes the production of the 10 vaccines approved by WHO for emergency use as of April 2022. Unless indicated otherwise, our analysis is based on the data provided by the COVID-19 Market Dashboard.²

Production capacity varies widely between vaccines. In early 2021, the PRC rapidly emerged as the largest producer, led by their Sinovac and Sinopharm vaccines (Airfinity 2021). However, the efficacy of their vaccines was questioned when newer variants emerged, leading to a much slower growth in new contracts over time. For example, the growth of new contracts for non-PRC vaccines expanded by about 10% from September 2021 to March 2022, whereas the figure for PRC vaccines was only 1% (Airfinity 2022). Pfizer–BioNTech and Moderna are expected to produce the most doses in 2022, enabling them to see the most revenue increase compared to other vaccines, thanks to higher demand and costs for their vaccines.

In addition to higher vaccine efficacy, another key factor that led to the stronger growth of non-PRC vaccines is their ability to scale up production. Much of the production capacity increase has been facilitated by vaccine partnerships. Some examples of key partnerships include SII with AstraZeneca and Novavax, Pfizer and GSK, and Janssen and Merck (Airfinity 2022). Splitting up the vaccine value chain, particularly between the two key stages of drug substance production and fill-and-finish, lies at the heart of vaccine manufacturing (Bown and Bollyky 2022). This process ultimately affects how many doses, how quickly, and where vaccines are produced.

Four main features can be identified from the production activities of leading vaccines. First, the growth of COVID-19 vaccine production capacity has been facilitated by the addition of vaccine manufacturers

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² The COVID-19 Market Dashboard (accessed in February 2022), maintained by the United Nations Children’s Fund (UNICEF), is a public resource that provides the latest information on the world’s COVID-19 vaccine market and COVAX vaccine deliveries.
at different stages of the vaccine supply chain (Figures 7.1 and 7.2). The growth is most rapid between 2020 and 2021, as key major vaccine developers had to increase their production capacity. Figure 7.1 shows that all the major vaccine developers generally doubled the number of their manufacturers, with Pfizer–BioNTech recording the highest growth (Bown and Bollyky 2022). This rapid increase explained why Pfizer–BioNTech dominated the production capacity in 2021 and is also forecasted to do so in 2022. Based on the Duke University Global Health Innovation Center, the forecasted 2022 production capacity, as of April, will be primarily driven by Pfizer–BioNTech (4 billion doses), Moderna (3 billion doses), and Oxford–AstraZeneca (2.4 billion doses). The rapid expansion of production capacity results from vaccine developers’ extensive use of outsourced contracts with external manufacturers. Note from Figure 7.2 that the increased production capacity was based more on CDMOs and technology transfer contracts than on vaccine developers’ own facilities. The use of outsourced contracts to increase the agility and capacity of production has been a crucial factor behind the global attempt to vaccinate their population.

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3 The data for December 2020 and June 2021 are based on Bown and Bollyky (2022) who analyzed the production chains of six vaccines: Pfizer–BioNTech, Moderna, AstraZeneca, Janssen, Novavax, and CureVac. However, Figures 7.1 and 7.2 do not include CureVac as it has yet to be approved for emergency use by WHO. For the February 2022 data, we rely on data of 10 WHO-approved vaccines available on the UNICEF COVID-19 Market Dashboard: Pfizer–BioNTech, Moderna, Oxford–AstraZeneca, Janssen, Novavax, Bharat Biotech, Sinovac, Sinopharm, Covishield, and Covovax. However, Figures 7.1 and 7.2 show only details of eight vaccines, as the latter two are both produced by SII and their production activities are included under AstraZeneca and Novavax.

4 The Duke University Global Health Innovation Center launched a Speedometer Initiative to aggregate and analyze publicly available data on COVID-19 vaccines and therapeutics. Their data can be accessed at https://launchandscalefaster.org /COVID-19.
Figure 7.1: Growth of COVID-19 Vaccine Production by the Number of Manufacturers of Each Vaccine

COVID-19 = coronavirus disease.

Sources: Created using data from Bown and Bollyky (2022) for the number of manufacturers in December 2020 and June 2021; and the UNICEF COVID-19 Market Dashboard for February 2022.

Figure 7.2: Type of Contract and type of Activity for Vaccine Manufacturers

CDMO = contract development and manufacturing organization.

Note: Data as of February 2022.

Source: Created using data from the UNICEF COVID-19 Market Dashboard.
Second, a closer look at the type of manufacturing activity of these vaccine manufacturers reveals that the largest increase over the past 2 years comes from the end-to-end or fill-and-finish stage, followed by drug substance production (Figure 7.3). These two stages lie at the heart of vaccine manufacturing, and both require high fixed costs of setting up specialized facilities and capital investment (Bown and Bollyky 2022). With the fill-and-finish stage being closer to vaccine distribution yet less sophisticated in its specialization, the increase in the number of contracted relationships is highest for this stage.

Third, despite the swift expansion of manufacturing capacity, vaccine production remains geographically concentrated. As discussed earlier, key players and activities in the vaccine value chains have been concentrated among the 13 countries of the “Vaccine Club” (Evenett et al. 2021). Production activities are highly concentrated; around 55% of capacity is in East Asia, 40% in Europe and North America, and less than 5% in Africa and Latin America (CEPI 2021). The vaccine production networks are, in general, global and have been built by collaborations through CDMOs and technology transfers. A 2020 survey by the Coalition for Epidemic Preparedness Innovations to estimate the vaccine manufacturing capacity revealed similar findings regarding the
geographical concentration of vaccine production. India has the largest production capacity for drug substances, followed by Europe and North America. Europe has the largest production capacity for RNA-based drug substances (Table 7.1). For drug products, the base-case estimates showed that the PRC has the largest production capacity, followed by North America and the rest of Asia and Oceania. Figures 7.4 and 7.5 show the locations with the highest number of vaccine manufacturers. What is evident from these two figures is that manufacturing activities in key locations are diverse, covering all stages of vaccine production and comprising a broad range of organizational forms—from own facilities to externalized contracts. The US, for example, is the single most important country for vaccine production activities, from drug substance production to fill-and-finish activities. The same is true for major vaccine-producing countries like Germany, India, the PRC, and the United Kingdom, confirming the geographically concentrated nature of vaccine production.

### Figure 7.4: Top Vaccine Production Locations by Production Type

<table>
<thead>
<tr>
<th>Country of production</th>
<th>Drug substance</th>
<th>End-to-end</th>
<th>Excipient supplier</th>
<th>Fill-finish</th>
<th>Fill-finish/end-to-end</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Germany</td>
<td>14</td>
<td>3</td>
<td>1</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>India</td>
<td>8</td>
<td>5</td>
<td>15</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>PRC</td>
<td>7</td>
<td>1</td>
<td>14</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>7</td>
<td>1</td>
<td>14</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Italy</td>
<td>5</td>
<td>1</td>
<td>14</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Japan</td>
<td>5</td>
<td>1</td>
<td>14</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Spain</td>
<td>5</td>
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<td>14</td>
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<td>France</td>
<td>4</td>
<td>1</td>
<td>14</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Belgium</td>
<td>3</td>
<td>3</td>
<td>14</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Brazil</td>
<td>3</td>
<td>3</td>
<td>14</td>
<td>12</td>
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<tr>
<td>Egypt</td>
<td>3</td>
<td>3</td>
<td>14</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Netherlands</td>
<td>3</td>
<td>3</td>
<td>14</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Republic of Korea</td>
<td>3</td>
<td>3</td>
<td>14</td>
<td>12</td>
<td>0</td>
</tr>
</tbody>
</table>

PRC = People’s Republic of China.

Note: Data as of February 2022.

Source: Created using data from UNICEF’s COVID-19 Vaccine Market Dashboard.

## Table 7.1: Geographical Locations of Vaccine Production Activities

<table>
<thead>
<tr>
<th>Regions</th>
<th>Adjuvant</th>
<th>Drug Substance</th>
<th>End-to-End</th>
<th>Excipient Supplier</th>
<th>Fill-Finish</th>
<th>Fill-Finish/End-to-End</th>
<th>Grand Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>14</td>
<td>2</td>
<td>7</td>
<td>26</td>
<td>2</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>Asia and the Pacific</td>
<td>4</td>
<td>15</td>
<td>2</td>
<td>15</td>
<td>1</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>8</td>
<td>3</td>
<td>3</td>
<td>13</td>
<td>2</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>South/Latin America</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>7</td>
<td>1</td>
<td>7</td>
<td></td>
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<tr>
<td>Africa</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Middle East</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
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<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Created using data from the UNICEF COVID-19 Market Dashboard.

CDMO = contract development and manufacturing organization, PRC = People’s Republic of China.

Note: Data as of February 2022.
Fourth, while awareness to increase the global production capacity has been heightened because of the pandemic, vaccine production activities reflect firm-level strategies of vaccine developers more than government policies. Vaccine producers can be loosely categorized into two manufacturing approaches, a globally distributed approach versus a centralized, in-house one. Most fall somewhere in the middle, but there are clusters of differences at both ends of the spectrum. Table 7.2 shows how different vaccine developers organize their production chains regarding types of contracts and geographical locations.

<table>
<thead>
<tr>
<th>Vaccine Developer</th>
<th>Africa</th>
<th>Asia and the Pacific</th>
<th>Europe</th>
<th>Middle East</th>
<th>North America</th>
<th>South/Latin America</th>
<th>Unknown</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer BioNTech</td>
<td>3</td>
<td>2</td>
<td>20</td>
<td>4</td>
<td>1</td>
<td>30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fill-finish</td>
<td>1</td>
<td></td>
<td>11</td>
<td></td>
<td>1</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excipient supplier</td>
<td>1</td>
<td></td>
<td>4</td>
<td></td>
<td>2</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug substance</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-to-end</td>
<td>2</td>
<td></td>
<td>1</td>
<td></td>
<td>1</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>9</td>
<td></td>
<td>11</td>
<td>4</td>
<td>3</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fill-finish</td>
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<td></td>
<td>5</td>
<td></td>
<td>3</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug substance</td>
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<td>4</td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td>1</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fill-finish/end-to-end</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excipient supplier</td>
<td></td>
<td></td>
<td></td>
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<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderna</td>
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<td>66</td>
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<td>3</td>
<td>17</td>
<td></td>
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</tr>
<tr>
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<td>2</td>
<td></td>
<td>4</td>
<td>7</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
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<td></td>
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<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
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<td>8</td>
<td></td>
<td>4</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
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<td></td>
<td></td>
<td></td>
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<td>4</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Excipient supplier</td>
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<td></td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fill-finish/end-to-end</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Janssen Pharmaceuticals</td>
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<td></td>
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<td></td>
<td>5</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fill-finish</td>
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<td>4</td>
<td></td>
<td>2</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug substance</td>
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<td></td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-to-end</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

continued on next page
Filling Finish: 1 7 1 1 1 12
Fill-finish/end-to-end: 1 1 1 2
End-to-end: 1
Sinovac
Fill-finish: 1 3 2 6
Fill-finish/end-to-end: 3 2
End-to-end: 1
Bharat Biotech
End-to-end: 3 1 4
Drug substance: 3
Fill-finish: 1 1 2
Total: 6 37 51 4 27 7 1 133
Source: Created using data from the UNICEF COVID-19 Market Dashboard.

Pfizer–BioNTech, Moderna, Janssen (Johnson & Johnson), and Sinopharm lean more toward a centralized approach. These vaccine makers are keeping manufacturing largely in-house and working with one or two big partners. Their manufacturing tends to be concentrated in one or two regions globally (Taylor et al. 2021). Pfizer–BioNTech may not control all the production activities internally but rely heavily on their existing plants and facilities to undertake drug substance production, resulting in their concentrated production facilities being concentrated in the US and the European Union (Bown and Bollyky 2022). It took much longer for Pfizer–BioNTech to consider setting up production facilities elsewhere. Their decisions to expand production capacity outside the US and the European Union only came in 2021 when BioNTech decided on setting up a new manufacturing facility in Singapore and more partnerships in the PRC and South Africa. Although BioNTech has unveiled plans to establish turnkey modular production facilities in shipping containers that could be transported to other regions, particularly Africa, the production capacity of 50 million doses is a fraction to the 1.2 billion doses of its production unit in Marburg, Germany, in 2021 (Aljazeera 2022). Similarly, Moderna, another mRNA vaccine maker, also relied heavily on contract partners to ramp up their production facility. Moderna teamed up with global CDMO partners to benefit from their capacity in the US and Europe. Moderna also partnered
with Samsung Biologics in the Republic of Korea for fill-and-finish activities to increase their coverage in Asia (Bown and Bollyky 2022; Taylor et al. 2021). The production strategy of these two mRNA vaccine makers remains concentrated geographically, with most activities located in North America and Europe. The lack of sufficient capabilities to undertake a new technological vaccine platform and the need for mRNA vaccines to be kept and transported in ultra-cold temperatures present challenges for the broader geographical distribution of its production facilities and contribute to the geographical concentration of these two vaccines’ production facilities.

Vaccines based on more traditional technology platforms, such as viral vector, protein subunits, and inactivated virus, face fewer challenges in engaging external partners across geographical locations. With a strategy that focuses more on creating different regional supply chains, Oxford–AstraZeneca stands out as the vaccine producer with the most geographically diverse locations, extending beyond the US and Europe to Australia, India, Latin America, and Southeast Asia (Bown and Bollyky 2022). The geographical diversification also reflects Oxford–AstraZeneca’s distribution strategy of supplying vaccines to a wider range of countries, particularly middle-income ones. Based on Duke Global Health Innovation Center’s data on total purchase classification by country income level, Oxford–AstraZeneca is the vaccine maker that puts the strongest emphasis on supplying middle-income countries and the global entity COVAX, which together account for more than 75% of its total doses procured. The ratio for Pfizer–BioNTech is only about 23%, as most of their doses procured are supplied to high-income countries. To understand how vaccine supply chains are established, these firm-level strategic differences also need to be considered.

7.3.3 Asia and the Pacific in COVID-19 Vaccine Value Chains

Countries in Asia and the Pacific are faced with the “triple challenge” of pursuing equitable distribution of vaccines, ensuring successful vaccination rollouts, and developing agile manufacturing capacity to produce essential drugs and vaccines (Reform for Resilience Commission 2021). Although the region is relatively well-represented in the vaccine value chain, especially when compared to other developing regions like Latin America and Africa, its presence is largely dominated

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6 See Duke Global Health Innovation Center Launch and Scale Speedometer web page.
by India and the PRC. Both countries rank among the top four producers of COVID-19 vaccines in January 2022, with the PRC’s total production capacity (locally administered and exported) approaching 5 billion doses, followed by the European Union (approximately 2.5 billion doses), India (approximately 1.8 billion doses), and the US (1.1 billion doses), according to Airfinity data cited in a report on vaccine production presented by the Global Commission for Post-Pandemic Policy (2022). However, non-Chinese ones are taking more market share from the less effective Chinese vaccines, with the growth of new contracts much slower for Chinese vaccines. The growth rate of new contracts for non-Chinese vaccines from October 2021 to March 2022 averaged over 10%, whereas the rate for Chinese ones was 1% (Airfinity 2022).

Table 7.3 provides details on COVID-19 vaccine manufacturing activities in Asia and the Pacific. The region’s participation in vaccine value chains can be broadly classified into two approaches depending on the role domestic companies undertake. Through CDMO and technology transfer contracts, larger and more experienced local companies may join with established pharmaceutical multinationals from developed economies to be part of their global vaccine production. For example, Oxford–AstraZeneca has engaged several pharmaceutical and biotechnology companies in Australia, India, Japan, the PRC, the Republic of Korea, and Thailand to scale up their production capacity. The Swedish-UK pharmaceutical multinational is probably the vaccine producer with the most extensive networks of regional companies in Asia and the Pacific, covering long-established contract manufacturers like Samsung Biologics or SK Bioscience in the Republic of Korea, as well as relatively newer companies like Siam Bioscience in Thailand. Pfizer–BioNTech, Moderna, and Janssen have also established contract partners in the region. Limited details are available on the precise nature of many of the manufacturing arrangements, but they range from arrangements covering purely bulk substance production or fill-and-finish to full process manufacturing (Table 7.2). Some, but still a small proportion, are also reported to include licensing and distribution rights.7

The most notable example of a contract company in the region is India’s SII. Considered to be the world’s largest vaccine manufacturer by volume, SII produces 1.5 billion WHO-approved jabs a year for diseases such as poliomyelitis, diphtheria, measles, mumps, and rubella for use by the public immunization programs of about 170 countries (Kazmin 2021). SII has been granted the right to manufacture the

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7 Data on COVID-19 vaccine manufacturing are presented in Global Health Centre (2022).
From Lab to Jab: Improving Asia and the Pacific’s Readiness to Produce and Deliver Vaccines

Oxford–AstraZeneca vaccine under the name Covishield for developing countries through COVAX, the United Nations-backed alliance. Given its production capacity, SII has also been granted the right to manufacture the Novavax vaccine starting in June 2021. However, the devastating wave of infections in India in March 2021 prompted the Government of India to ban exports from SII and to divert all of its production to domestic use, causing the company to miss its export commitment during March to late November 2021 (Aljazeera 2021).

In addition to serving as contract manufacturers for leading pharmaceutical multinationals, research institutes and companies in Asia, particularly those in India and the PRC, have also developed their own COVID-19 vaccines. Covaxin, developed by India’s Bharat Biotech, Sinovac, and Sinopharm are among the vaccines that WHO has approved for emergency use. While Bharat Biotech limits its production facilities only in India, Sinovac and Sinopharm also contract out part of their manufacturing activities to other middle- and low-income countries in the region. Sinopharm has set up fill-and-finish operations

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8 On 2 April 2022, WHO confirmed the suspension of supply of Covaxin (Bharat Biotech) through United Nations procurement agencies and recommended that countries using the vaccine take action as appropriate. The suspension is in response to the outcome of a WHO inspection on 14–22 March 2022, and the need to conduct process and facility upgrade to address recently identified deficiencies in good manufacturing practices. See WHO (2022) departmental news.

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Table 7.3: Type of Partnerships across Geographical Locations

<table>
<thead>
<tr>
<th>Regions</th>
<th>CDMO</th>
<th>Own Facility</th>
<th>Technology Transfer</th>
<th>Grand Total</th>
</tr>
</thead>
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<tr>
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<td>43</td>
<td>5</td>
<td>3</td>
<td>51</td>
</tr>
<tr>
<td>Asia and the Pacific</td>
<td>9</td>
<td>10</td>
<td>18</td>
<td>37</td>
</tr>
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<td>4</td>
<td>2</td>
<td>27</td>
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<td>South/Latin America</td>
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<td></td>
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</tr>
<tr>
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<td>4</td>
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<tr>
<td>Unknown</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

CDMO = contract development and manufacturing organization.
Source: Created using data from the UNICEF COVID-19 Market Dashboard.
in Bangladesh, Myanmar, and Singapore, while Sinovac’s contract partners are located in Indonesia, Malaysia, and Sri Lanka. The practice of contracting other manufacturers in similar income-level countries is common for vaccine developers from middle-income countries such as the PRC, Cuba, India, Kazakhstan, the Russian Federation, and Viet Nam. This pattern is different for vaccine developers from high-income countries, which primarily select manufacturing partners in other high-income economies (Global Health Centre 2022). Although increasing vaccine manufacturing capacity through regional participation in vaccine value chains is one way to ensure access to vaccines, it may not solve issues of equitable vaccine distribution. The next part explores bottlenecks and challenges in vaccine production and discuss policy directions in further details.

7.3.4 Challenges in Vaccine Production

Since the first cases were reported in Wuhan, PRC, in December 2019, the world has seen unprecedented progress in COVID-19 vaccine development, production, deployment, and distribution. Vaccine manufacturers and their suppliers have been scaling up vaccine production from zero to billions of doses, with a forecasted accumulated supply of over 18 billion doses by the end of 2022.⁹ This represents three to four times the pre-pandemic annual demand for all vaccines of 5 billion doses (Airfinity 2021). Nonetheless, the vaccine production process is far from smooth, and too many bottlenecks still prevent vaccine manufacturers from achieving their targets. We classify these challenges and obstacles into three broad categories: those facing vaccine supply inputs, those inhibiting the vaccine production processes, and policy and regulatory issues.

First, the scale-up of manufacturing capacity is subject to mitigating upstream supply challenges in securing critical inputs in raw materials, consumables, and equipment across the vaccine value chain (Taylor et al. 2021). While some of these inputs are specific to a vaccine technological platform, others (e.g., glass vials) are common across all types of vaccines. Many of these inputs are provided by a limited number of supplier bases that also face significant demand peaks from the outbreak of COVID-19. The limited data to forecast manufacturing needs, on top of the lack of visibility on the supplier base, increase potential supply constraints on these crucial inputs. Long-term demand uncertainties

⁹ The UNICEF COVID-19 Market Dashboard forecast the 2022 low case total supply at 16.8 billion doses, base case at 18.7 billion, and high case at 20.9 billion.
for these inputs also add to the challenges of investment decisions and capacity expansions.

Second, scaling up vaccine production capacity faces challenges in both establishing new facilities and repurposing existing ones for COVID-19 vaccine production. Each vaccine technology platform faces its own challenges in scaling up quickly due to the novelty of COVID-19 vaccine technology. The traditional way of growing cell cultures in bioreactors requires time and careful management to grow and keep live cells healthy and thriving. Vaccine makers who rely on live cultures also struggle with yields, making it harder to make vaccines fast and in large quantities. Scaling up this production stage in newly established facilities makes it even more challenging, as seen in the struggle AstraZeneca faced in meeting its production targets in early 2021. The company said it could take 6–9 months to start a production site from scratch, and that timetable was possible only by working with experienced partners at an accelerated pace (Economist 2021).

Similarly, ramping up the production of mRNA vaccines also has its own challenges. Supplies of raw materials needed in the process of vaccine production, such as nucleotides, or the fatty bubbles that are required to protect the mRNA molecules, are limited. Before using mRNA technology for COVID-19 vaccines, these materials were used more specifically in niche cancer treatment. New production capacity that needs to be set up to meet the demand for COVID-19 vaccines in addition to other usage presents an additional challenge to take into consideration. Before this pandemic, no networks of contract manufacturers existed for several of the leading vaccine candidates that feature novel technologies, including those relying on mRNA delivery platforms (Wouters et al. 2021).

On top of setting up new facilities or repurposing existing ones, another crucial constraint to rapid capacity expansion is the requirement for widespread technology transfer. Few countries have the domestic capacity to produce COVID-19 vaccines rapidly and independently. Therefore, a successful global production capacity expansion will require intensive and active knowledge sharing, technology transfer, and data visibility along the vaccine value chain. Doing all these in normal times is already time-consuming but having to manage intensive technology transfer when many countries impose travel restrictions adds another layer of challenges to the scaling up of COVID-19 vaccine production. Setting up vaccine production facilities is also costly. They pose a crucial barrier to vaccine production expansion in emerging economies.

Successful technology transfer also requires technical competence and a skilled workforce. The ability to hire, train, and develop quality
personnel is a challenge even for highly experienced manufacturers. A strong scientific and technical workforce base with know-how in vaccine-specific manufacturing and quality control systems is crucial in sustaining vaccine production. This requirement may not be such a challenge in advanced or large middle-income economies with sound technical and scientific education systems such as the PRC and India, but smaller economies that are new entrants to vaccine production may need to build a scientific ecosystem that can ensure sufficient development of the knowledge base (Plotkin et al. 2017). The need to rapidly scale up COVID-19 vaccine production across different geographical regions in a short period would pose challenges not just to vaccine developers but also to contract partners in different parts of the world.

Beyond production-specific requirements, policy and regulatory issues can also cause bottlenecks in vaccine production. Five key areas that need to be considered to enable the vaccine capacity expansion are (i) measures to ensure free flows of essential supplies, (ii) regulatory requirements on quality controls and manufacturing standards, (iii) agreements on collaborations, (iv) measures to increase financing, and (v) initiatives to increase data visibility along the vaccine value chain (Duke Global Health Innovation Center 2021). Vaccine manufacturing is an expensive, complex process, in which even subtle changes may affect the quality, safety, and ultimately efficacy of the final vaccine. That is why the process is tightly regulated, not just for the finished products, but for each stage of production and each facility where manufacturing occurs (Bollyky and Bown 2020). Not many companies in the world have the capacity to produce vaccines in billions of doses. Vaccines also need to meet national regulatory requirements in the markets to be administered. Complying with all these requirements could slow down the vaccine production process, requiring efforts to reduce these bottlenecks without jeopardizing the quality of the vaccines.

The globalized nature of vaccine value chains and their production makes it even more necessary for regulatory requirements to be enforced multilaterally and collaboratively. Imposing unilateral requirements or export bans can lead to disruptions in the supply chains of critical vaccine inputs as well as of vaccines. Regulatory restrictions like export bans may help those countries in stockpiling supplies in the short term, but they may unintentionally lead to adverse consequences in the longer term. For example, after the 6-month vaccine export ban India imposed in March 2021, SII had to reduce its production of the AstraZeneca vaccine. Not only did the procurement from the Indian government slow down as the country has reached its vaccination target, the company’s main buyer, COVAX, had to procure their supplies from elsewhere after the company failed to honor its earlier purchase agreement (Das 2021).
These are examples of policy and regulatory constraints that can pose challenges to vaccine production.

### 7.4 Conclusions and Policy Recommendations

This chapter explores the production of COVID-19 vaccines to draw insights and implications on the preparedness of Asia and the Pacific as a region. Prior to this pandemic, most countries seemed well served with existing systems to administer vaccines to their population to prevent the most common diseases. However, COVID-19 is an outlier event in the vaccine industry, rapidly spreading globally with high transmission and mortality rates. The race for a cure prompted wealthier countries to support and subsidize pharmaceutical firms in their research and development. The subsequent race for production also enticed some countries to constrain global distribution of ingredients and vaccines to prioritize their domestic markets. These beggar-thy-neighbor policies set dangerous precedents for global health policy directions.

Nevertheless, COVID-19 provides important lessons to understand how countries may be better prepared for the next pandemic. Regardless of vaccine technology platforms, achieving the complex vaccine manufacturing process without compromising on quality poses a wide range of operational challenges. Regulatory and policy issues need to address input supply challenges, and manufacturing capacity and interdependencies beyond COVID-19 vaccine stakeholders.

Policy discussion can be classified into two broad topics—scaling up supply inputs and manufacturing capacity, and enabling an efficient and effective ecosystem of vaccine production. The first area of policy issues is operation specific, addressing key questions such as how to increase the efficiency of existing capacity and how to repurpose existing capacity and add new capacity to handle the sudden demand spike. The second set of policy issues covers a wider range of issues that are crucial in enabling and strengthening longer-term supply capacity, including guaranteeing the free flow of goods, technical capacity, and production capacity; creating a regulatory system that can help improve the fungibility of supplies and the capacity of supply chains; encouraging collaborations across public and private stakeholders; implementing financing solutions that contribute to expanding and enhancing the vaccine and scientific ecosystem; and increasing value chain visibility to help various market participants and stakeholders make timely and effective decisions. The appendix to this chapter provides a decision tree for the actions that can be considered to prepare for the next pandemic.

The rapid emergence and diversity of COVID-19 vaccine value chains reflect the dynamic interaction of factors at different levels. The
broader context of the pandemic cannot be overlooked, as the early phase of vaccine shortage and disruption could hardly be anticipated. However, differences in the vaccine value chains also reflect contributing factors at different levels (Gereffi, Pananond, and Pedersen 2022). Firm-level considerations, such as vaccine technology platform, and vaccine developers’ marketing strategy on pricing and distribution channels, all play a part in how the vaccine value chain is constructed. In addition, global value chain governance also reflects factors specific to the vaccine value chain. How each developer wants to organize their value chain and which CDMO partners are available are all relevant to global value chain governance decisions. Last but certainly not least are country-level factors such as trade policy and the extent and direction of government subsidies. Given the complex nature and the interaction of these factors, making any generalized conclusion about vaccine manufacturing could come at one’s own peril.

A country’s readiness for vaccine production depends on an interaction of factors at the firm, value chain, and country levels. Taking part in vaccine production should not be a desirable goal and one to achieve at all costs. Instead, the goal of a country’s vaccine policy should focus first and foremost on full and rapid vaccination of the population with an effective system of vaccine production and distribution. Ensuring access to vaccines, regardless of where they are made, is the first step toward quick vaccination of the population to save lives and livelihoods. Next, policymakers should be reminded that the determining factor of a country’s readiness and ability to take part in the vaccine value chain is its technological capacity. The more complex the stage of vaccine production, the higher the need for technological capacity. Countries with limited technological capacity should focus first on ensuring effective and quick procurement and distribution of vaccines, while those with higher technological capacity should not shy away from collaborating with other companies in less developed economies to ensure a speedy global production and distribution.
References


Preparing for the Next Pandemic: Vaccine Global Value Chains and Local Production Capacity


and Factors to Consider when Planning the Establishment of a Vaccine Production Facility. New York, NY: UNIDO.
Appendix

Decision Tree for Pandemic Preparedness Vaccine Manufacturing

**Step 1.** Is there a new transmissible disease?

No: No action on production, invest in strengthening distribution channels for current treatments and vaccines.
Yes: Go to step 2.

**Step 2.** Does the new transmissible disease spread easily from person to person?

No: Isolate and treat sick people, contain cases (identify cases, limit exposure and travel), purchase additional personal protective equipment for health-care workers.
Yes: Go to step 3.

**Step 3.** Do existing treatments work well to treat the new easily transmissible disease?

No: Go to step 4.
Yes: Use existing treatments and order more from manufacturers and go to step 6.

**Step 4.** Are there untested treatments that could work to treat the new easily transmissible disease?

No: Go to step 5.
Yes: Collaborate with pharmaceutical firms to analyze efficacy of untested treatments and go to step 6.

**Step 5.** Could pharmaceutical firms develop new treatments to treat the new easily transmissible disease?

No: Isolate individuals to limit transmission and wait for the pandemic to run its course quickly.
Yes: Collaborate with pharmaceutical firms to analyze efficacy of untested treatments and go to step 6.

**Step 6.** Can pharmaceutical firms produce enough treatment quickly?

No: Go to step 7.
Yes: Contract with firms for the provision of treatment, negotiate price based on cost benefit analysis, invest in strengthening the distribution channels while treatment is being manufactured.
**Step 7.** Do pharmaceutical firms need a sophisticated manufacturing base in place to produce the treatment?

No: Negotiate with pharmaceutical firms to set up local production to scale up to the needs of the country and invest in strengthening the distribution channels while treatment is being manufactured.

Yes: Go to step 8.

**Step 8.** Does the country have an established and sophisticated production capacity for the new treatment?

No: Contract with pharmaceutical firms for the provision of treatment, negotiate price based on cost benefit analysis, invest in strengthening the distribution channels while treatment is being manufactured.

Yes: Negotiate with pharmaceutical firms to set up local production to scale up to the needs of the country and invest in strengthening the distribution channels while treatment is being manufactured.

Meanwhile, consider these initiatives as generic guidelines:

- Assess the global value chains of vaccines to identify gaps and shortages and to understand where participation is possible. A plan to manufacture can also consider the supply chains of key ingredients such as lipid particles, proteins, syringes, and vials.
- Consider bilateral, regional, or multilateral collaborations and contracts across the public and the private sectors to scale up production. For example, explore regional initiatives such as those launched by the Pan American Health Organization (PAHO) to boost vaccine production in Latin America, or other collaborations agreed under the Quad Vaccine Partnership.
- Consider bilateral, regional, or multilateral regulatory agreements on standards and controls over vaccine production and distribution to help facilitate and speed up the possibility of new regional manufacturing activities.
- Consider access to financing and financial support to accelerate public and private investment across the vaccine manufacturing and distribution ecosystem.
- Invest in education to enhance the overall skill levels in science and technology.
8

International Transport and Logistics of Vaccines across Borders: The Case of Asia and the Pacific

Rawinkhan Srinon, Duangpun Kritchanchai, and Thananya Wasusri

8.1 Introduction

At the very early stage of the coronavirus disease (COVID-19) pandemic in 2020, medical supplies such as personal protective equipment, surgical masks, and alcohol sanitizer posted many logistical challenges such as supply shortages, on-time delivery, and other issues. Raw material shortages and countries closing their borders have been some of the major difficulties in running a smooth supply chain. These concerns required both industry and the government to act quickly to boost supply and put measures in place to smooth cross-border procedures.

In late 2020, many vaccines were produced and approved under emergency use authorization. Although COVID-19 vaccines are demanded by all countries, not all can develop and produce them for many reasons and limitations (OECD 2021). Vaccine production, either of COVID-19 or other vaccines that are part of the Expanded Programme on Immunization (EPI), is commonly complicated, requiring specialized equipment and inputs, storage facilities, highly skilled labor,

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1 The study for this chapter was funded through a collaboration of the United Nations Economic and Social Commission for Asia and the Pacific (ESCAP) and the World Health Organization (WHO).

2 The objective of EPI is to progressively provide vaccines to ensure the immunization for vulnerable people before they develop infectious diseases.
and other capabilities. Therefore, only certain countries can generally produce vaccines and then export them across borders to different parts of the globe. Typically, cross-border importing of vaccines and vaccine inputs is often more complicated than exporting. The complex steps and requirements often cause bottlenecks and hurdles that result in delays.

This chapter aims to better understand the delivery of vaccines in Asia and the Pacific, with a focus on questions related to cross-border cooperation and transport. The findings of our research should help developing countries in the region improve vaccine transport connectivity and better prepare for the next pandemic, as well as fight against other communicable diseases.

### 8.1.1 COVID-19 Vaccine Cold Chains

New vaccines typically take approximately more than 10 years to develop and receive approval. However, COVID-19 vaccines have been approved in a short period following a “pandemic paradigm” (WTO 2020). Yet, the timeline of developing COVID-19 vaccines was significantly shorter because of the global pandemic and emergency use authorization. While vaccine production is often located in only a small number of countries, supplies of some vaccine inputs are also concentrated in a few others. As stated by Frank Appel, Chief Executive Officer of Deutsche Post DHL Group, “Vaccines are in development, but their ability to end this pandemic depends on an effective supply chain that can connect diverse production locations to the public” (WTO 2020). Secure and timely delivery affects the efficiency of vaccine production and distribution. Figure 9.1 shows the international COVID-19 vaccine supply chain from the import of vaccine inputs by manufacturers to the transport of vaccines across borders to destination countries for immunization.

At each point in the vaccine supply chain, international transport and logistics, including regulations and customs clearance, are challenging.

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**Figure 8.1: International COVID-19 Vaccine Supply Chain**

![Diagram of the international COVID-19 vaccine supply chain](source)

COVID-19 = coronavirus disease.

Source: Author’s illustration.
Another noteworthy concern to ensure vaccine quality and efficacy is the cold chain. Most countries are familiar with EPI vaccine cold chains, which traditionally require a temperature range of 2°C to 8°C. However, COVID-19 vaccines were developed with diverse technologies, and they need to be transported and kept at different temperatures. For example, viral vector vaccines produced by Janssen and AstraZeneca can be kept at the traditional cold chain range, while the mRNA vaccine produced by Pfizer–BioNTech must be stored at approximately –70°C and the mRNA vaccine produced by Moderna at approximately –20°C. As a result, most countries are not familiar with and do not have enough capacity for ultra-cold chain systems (–80°C to –70°C) and frozen cold chains (–20°C to –15°C). For lower-income countries in Asia and the Pacific, the main issue is lack of capacity for cold chain storage area while transporting COVID-19 vaccines across borders. Thus, increasing cold chain capacity for mass immunization poses significant challenges for lower-income countries. Cold chain capacity deficiency affects procurement and transportation and cross-border logistics efficiency. It could result in suppliers not releasing vaccines from their warehouses for international shipment, risking cold chain breach during cross-border transport.

8.1.2 Cold Chain Facilities

COVID-19 vaccines require different temperatures ranging from –80°C to 8°C for storage and distribution. Different equipment such as freezers, refrigerators, cold boxes, and refrigerated trucks are needed to ensure perfect conditions for the vaccines from one end to the other end of the supply chain at each level of the vaccine cold chain system. Moreover, different temperature monitoring devices such as vaccine vial monitors, electronic temperature loggers, and electronic freeze indicators are necessary to monitor vaccine temperature as well as the data tracking and tracing systems.

Country cold chain facilities for both conventional cold chains (2°C to 8°C) and frozen to ultra-cold chains (as low as –80°C) are needed. Vaccines are shipped out in different quantities, requiring readiness of different storage and handling equipment during the shipment. This requirement impacts the international transport and logistics of COVID-19 vaccines. They are also relevant to releasing vaccines from manufacturers’ warehouses and the possible availability of the vaccines and vaccine wastage. The ultra-cold chain freezers are also in high demand and may not be available in the existing national health system and/or immunization program of low- and middle-income countries. Besides having the equipment, getting it to work properly is undeniably another challenge.
According to measured levels of preparedness for cold chain capacity (Figure 8.2), most economies in the Pacific and Central Asia do not have enough capacity to handle both conventional cold chains and ultra-cold chains, as the level of preparedness for cold chain logistics is low at level 1 (ADB 2021). Meanwhile, higher-income economies such as New Zealand, Australia, Japan, and the Republic of Korea and one upper middle-income country, the People’s Republic China (PRC), could manage cold chain integrity as they have high levels of preparedness for conventional cold chains (level 5) and for ultra-cold chains (level 4). WTO (2021) also noted that low- and middle-income economies will need to invest more on cold chain capacity to handle higher-volume shipments, especially for ultra-cold storage.

Figure 8.2: Measure of Preparedness for Cold Chain Logistics in Asia and the Pacific

PRC = People’s Republic of China.

Note: Preparedness is ranked from 1 (lowest) to 5 (highest). Blue lines represent traditional cold chains (2°C to 8°C), and orange lines represent ultra-cold chains (as low as -80°C).

Source: Adapted from ADB (2021).

Moreover, the lack of a proper storage system in remote locations might also lead to a delay in vaccine delivery, which in turn may also reduce the effectiveness of the COVID-19 vaccine supply chain (Rosen, Waitzberg, and Israeli 2021). Israel, with a population of 9.3 million, had administered more COVID-19 vaccine doses than all economies aside from the PRC, the US, and the UK. Moreover, Israel had administered almost 11.0 doses per 100 population, while the next highest rates were
3.5 doses per 100 population in Bahrain. In addition, some COVID-19 vaccines are extremely temperature-sensitive, so an inability to maintain the recommended temperature while transferring vaccines from manufacturers to consumers, especially with the vaccine supply chain in tropical regions, may lower vaccine efficacy (Lin, Zhao, and Lev 2020). Insufficient skills, knowledge, and management capacity can also lead to vaccine wastage (ADB 2021).

Cases of vaccine cold chain management in several economies in Asia and the Pacific are demonstrated in the following section, as well as good practices of Malaysia, Singapore, and Thailand.

8.2 Methodology

Since COVID-19 broke out in late 2019, we collected research data and information from 2020 to 2022. We started by conducting desk reviews, basically of the background and pandemic situations, our scope, and refining the focus. Two sources of information were considered: up-to-date reports and academic publications. The reports are from both the public and private sectors. The academic papers were selected based on current situations and case studies from countries.

Once we were able to structure the findings from the desk reviews, we then identified our focus areas and issues. Semi-structured interviews of Thai stakeholders were conducted from November to December 2021. We asked three main questions on (i) current process flows; (ii) key activities including pre-shipment, shipment, and post-shipment; and (iii) issues and pain points with respect to the process flows and activities. The interviewees included a cargo and warehouse director of Thai Airways; a product director of the Government Pharmaceutical Organization (GPO), which acts as Thailand’s importer and distributor; pharmaceutical distributors who act as logistics service providers; the customs department at Suvarnabhumi International Airport in Bangkok; and Food and Drug Administration (FDA) officials.

Following our data collection, we conducted a systematic analysis to illustrate major challenges and stakeholders’ policy recommendations, with the roles and responsibilities mapped to the stakeholders in detail.

8.3 Inadequate Cold Chain Capacity Case Examples in Asia and the Pacific

In Bangladesh, 26 ultra-low temperature freezers delivered by UNICEF through COVAX in August 2021 are enabling the country to receive, store, and distribute large quantities of COVID-19 vaccines that require
ultra-cold storage. Over 300,000 doses are held by each freezer. This supports administration of these vaccines in districts beyond the capital city, Dhaka. Having freezers delivered at speed and putting them to work was very challenging, again because of the need to re-gas the freezers. The shipment has boosted the country’s 26-freezer ultra-cold chain capacity to store almost 9 million vaccines (UNICEF 2021a).

Although the Universal Immunization Program of India provides free immunization across the country, participation is limited due to misinformation. The program also faces difficulty reaching isolated villages. Moreover, the percentage of immunized children is lower in rural areas. Around 8% of the program’s vaccines are wasted because of expiration and cold chain integrity problems. In rural areas, cold storage facilities can store about a month’s supply of vaccines and only a third of the facilities work properly (ADB 2021).

Indonesia, one of the countries benefiting from COVID-19 vaccine donations from COVAX, received 17 ultra-cold chain freezers in August 2021, funded by Gavi, the Vaccine Alliance, which hold a combined 3.5 million COVID-19 vaccines that require storage at up to –70°C. One of the challenges has been to deliver the freezers at speed and putting them to work, because they had to be re-gassed after the refrigerant gas had been removed before air shipment in accordance with airline safety protocols (UNICEF 2021b).

Vaccine shortages, limited funds, poor data, and cold chain capacity are the problems on the supply side in the Lao People’s Democratic Republic. These problems are more critical in rural areas than in urban areas. In addition, health workers reported that they had to use their own vehicles, usually a motorbike, to transport cold boxes and that they had difficulties balancing the box. This is one reason that vaccine campaigns cannot reach rural areas (ADB 2021).

Demand for vaccines is lower in rural areas in Pakistan because of cultural resistance and the limitation of the health infrastructure. Seven in 10 people live in rural areas, and about 40% of children below the age of 5 years in the country, especially in poor and rural areas, are not immunized or are under-immunized. Moreover, the immunization centers are not equally available throughout the country, and there is no proper cold chain monitoring and equipment maintenance, causing inefficiencies in the immunization schedule. The backup power source generally is insufficient to keep or maintain cold chain integrity (ADB 2021).

Cold chain capacity is limited in the Philippines. In January 2021, the country was preparing to use storage for meat and fish to handle vaccines (Calonzo 2021). The unpredictable weather and poor infrastructure of the country add to problems in accessing rural and remote areas. The
lack of backup power sources in rural areas lead to unstable power supply for refrigerators of health centers. Similarly, the lack of skilled personnel leads to vaccine wastage (ADB 2021). The Government of Australia in January 2022 supported the country’s COVID-19 vaccine scale-up efforts, through the United Nations Children’s Fund (UNICEF) Philippines, by officially providing cold chain equipment to help address gaps in storage capacity at all levels of the national health system (UNICEF 2022). UNICEF Philippines procured 30 solar-powered vaccine refrigerators and eight walk-in cold rooms.

Singapore’s international airport acts as the centralized warehouse for COVID-19 vaccines with its 18 cold storage rooms, temperature-controlled truck docks, and active temperature-controlled containers. This makes Singapore a leader in Southeast Asia in cold chain system management, particularly for ultra-cold chains. Cool dollies were designed to secure the movement of products in a temperature-controlled system. This new temperature-controlled dolly will not only protect temperature-sensitive vaccines such as those developed by Pfizer–BioNTech (Comirnaty) and Moderna from spoilage, but can also further enhance Singapore airport’s status as a reliable and quality air hub for pharmaceutical and perishable supply chains (Khanzada 2021).

Thailand prepared to implement a vaccine cold chain system since the beginning of the COVID-19 pandemic in early 2020. The collaboration between the government and the Federation of Thai Industries has been closely established. Freezers, cold boxes, Internet of Things-based temperature monitors, wi-fi services, and backup power sources were installed throughout the country. In addition to this collaboration in terms of cold chain facilities, which was initiated, the Ministry of Public Health, the Federation of Thai Industries, hospitals, logistics service providers, the national research funding agency, and Mahidol University are collaborating to implement a real-time tracking and tracing system to monitor an end-to-end vaccine cold chain. This system allows monitoring of the status of vaccines in real time, providing useful information on temperature, location, vaccine name, manufacturing site, production lot or batch, expiry date, injection date, and other related records.

Table 8.1 summarizes the major hurdles and bottlenecks encountered in some countries in Asia and the Pacific.
Table 8.1: Examples of National Hurdles and Bottlenecks with COVID-19 Vaccine Cold Chain Capacity

<table>
<thead>
<tr>
<th>Country</th>
<th>Hurdles and Bottlenecks</th>
</tr>
</thead>
</table>
| India                                  | - Expiry and problems in the cold chain  
- Limited cold storage facilities       |
| Indonesia                              | - Insufficient of ultra-cold chain facilities                                          |
| Lao People’s Democratic Republic       | - Vaccine shortages  
- Lack of funds  
- Poor data  
- Poor cold chain management and cold chain facilities |
| Pakistan                               | - Cultural resistance  
- Limited health infrastructure  
- Lack of cold chain monitoring  
- Inadequate backup power source to support cold chain integrity |
| Philippines                            | - Insufficient cold chain facilities  
- Intermittent power supply for refrigerators of health centers in rural areas with no backup power source |

COVID-19 = coronavirus disease.


8.4 Existing Process of Cross-Border Vaccine Transport in Asia and the Pacific

8.4.1 Procedures and Stakeholders of Cross-Border and International Logistics of COVID-19 Vaccines

Figure 8.3 illustrates cross-border flows of COVID-19 vaccines, starting from inbound vaccine inputs to outbound finished vaccines. The figure is based on our in-depth interviews with Thailand’s GPO, which oversees the importation of COVID-19 vaccines, the Thai customs agency, Thai Airways, the country’s FDA, and major professional pharmaceutical distributors, as well as literature review of related research or working papers (e.g., DHL 2020; ADB 2021; WCO 2021).

To import COVID-19 vaccines, companies need to be authorized as importers of these vaccines by the regulator, such as the FDA. The vaccine demand from government and other related information
(e.g., vaccine name, manufacturing sites, laboratory tests, labeling, and packaging) must also be approved. Then, purchase orders can be placed to vaccine developers and vaccine manufacturers. To produce the vaccines, manufacturers import raw materials and packaging materials in line with customer demand. Once vaccine samples pass all standard tests, a lot release can be issued. When vaccines arrive at a port of entry, the temperature during transport and the sealing of the package are checked. The customs clearance authority checks the documents according to the cross-border procedure, either with or without physical inspection of the shipment. For COVID-19 vaccines, customs clearance was initially conducted without physical inspections to speed up the process and protect the vaccine temperature integrity. Vaccines are then immediately transferred to a central warehouse to properly maintain their temperature. Table 8.2 and Figure 8.4 show the pre-shipment, shipment, and post-shipment activities, indicating potential delays.
## Table 8.2: Key Activities in International Transport and Logistics of Vaccines and Vaccine Inputs

<table>
<thead>
<tr>
<th>Pre-shipment</th>
<th>Shipment</th>
<th>Post-shipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Negotiation and procurement</td>
<td>• Coordination and facilitation between flight, airport terminal, customs clearance, and transport</td>
<td>• Check of temperature during transport and package seal</td>
</tr>
<tr>
<td>• Food and Drug Administration (FDA) application for vaccine license</td>
<td>• Shipment and documents for clearance</td>
<td>• Checklist of FDA at port of entry of vaccine, quality, and release for customs clearance</td>
</tr>
<tr>
<td>• Confirmation of goods and product specifications</td>
<td>• Security measure to ensure shipment from counterfeiting and theft</td>
<td>• Vaccine efficacy check and testing for compliance with lot release&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>• Documentation for customs clearance and communication with airport terminal (cold room)</td>
<td></td>
<td>• Transport to country-level warehouse</td>
</tr>
<tr>
<td>• Arrangement of transportation (flights, cold chain-compliant trucks)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Communication and engagement with all related stakeholders</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Lot release is a mechanism that enables the FDA to continuously monitor the quality of several biological products in real time through review and testing.

Sources: Adapted from World Customs Organization (2021) and in-depth interviews.
FDA = Food and Drug Administration, WHO = World Health Organization.

Note: The blue star marks indicate activities where delays could potentially take place.

Sources: Adapted from World Customs Organization (2021) and in-depth interview with stakeholders.
8.4.2 Issues in Cross-Border and International Logistics of COVID-19 Vaccines and Vaccine Inputs

COVID-19 vaccines have been gradually rolled out since the end of 2020, but the logistics of the vaccines are sophisticated and remain challenging. During the pandemic, air transport capacity was massively reduced because of airport closures and the lack of commercial flights. About 8,000 cargo jumbo jets would have been needed to deliver the vaccines for 7.8 billion people worldwide, but only 400 flights were available in 2020 (ADB and ESCAP 2021). According to our two in-depth interviews in November and December 2021 with a major pharmaceutical distributor who has been handling international logistics and transport of Moderna and Pfizer–BioNTech vaccines, it was especially difficult to reserve a flight to transport COVID-19 vaccines due to flight limitations during the early phase of the pandemic. Frequent or reliable flights should be a priority to minimize chances of flight cancellation. If a direct flight is not available, the shortest indirect transit flight via qualified transit airports should be used to ship the vaccines. While the customs clearance procedure for COVID-19 vaccines is conducted without physical inspection to reduce the customs lead time and to maintain the vaccine temperature, vaccine inputs are treated as normal products or non-priority products (WTO 2021). Moreover, the last-mile logistics and distribution operations to assure the temperature of COVID-19 vaccines are challenging as cold chain facilities are inadequate in some countries. Similar bottlenecks or “pain points” of COVID-19 vaccines in transport and logistics are illustrated in Figure 8.5.

While “green channels” have been applied for COVID-19 vaccines, vaccine inputs need to pass the customs clearance process under a regular control measure. In other words, neither green channels nor other simplified customs clearance procedures for vaccine inputs can be used (WTO 2021). As a result, the vaccine inputs could take about 5 working days to pass customs clearance in some countries (Table 8.3).

Additionally, new machines, facilities, or other materials that are necessary to build up vaccine production capacities took a long time to complete import and customs clearance procedures as import licensing needs to pass several approval processes. National lockdowns occasionally led to delays in obtaining consular documents or submitting necessary documents used for customs clearance procedures as some embassies and consulates closed down. Moreover, it was difficult to plan and manage imports of vaccine inputs as import and export restrictions were unpredictable in some countries (WTO 2021).

As imports of vaccine inputs must pass normal customs clearance processes, supply chain and customs clearance lead times for general cargo can be used to estimate those for vaccine inputs. The World Bank
Figure 8.5: Bottlenecks of Logistics and Distribution of COVID-19 Vaccines

COVID-19 = coronavirus disease.
Source: Adapted from DHL (2020).

Table 8.3: Airport Supply Chain Lead Time and Clearance Time in Selected Economies in Asia and the Pacific (no. of days)

<table>
<thead>
<tr>
<th>Region</th>
<th>Economy</th>
<th>Export — Lead Time</th>
<th>Import — Lead Time</th>
<th>Clearance Time without Physical Inspection</th>
<th>Clearance Time with Physical Inspection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oceania</td>
<td>New Zealand</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Australia*</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>East Asia</td>
<td>Korea, Rep. of *</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>China, People’s Rep. of *</td>
<td>2</td>
<td>6</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Japan*</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Hong Kong, China</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Taipei, China</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Mongolia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>Viet Nam*</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Thailand*</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Singapore</td>
<td>2</td>
<td>2</td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

continued on next page
(2018) has measured the supply chain lead time and clearance lead time for general cargo in its Logistics Performance Index. Export and import lead times are different for each economy (Table 8.3). Uzbekistan, a country with a COVID-19 vaccine manufacturing site, would take about 3 days to import general cargo and 1 day to pass customs clearance processes for both with and without physical inspection. It would take 5 days to import general cargo to Bangladesh, including 2 or 3 days to pass customs clearance processes, and only 1 day to Australia, with 1 or 2 days for customs clearance procedures. Comparing the import

<table>
<thead>
<tr>
<th>Region</th>
<th>Economy</th>
<th>Export Lead Time</th>
<th>Import Lead Time</th>
<th>Clearance Time without Physical Inspection</th>
<th>Clearance Time with Physical Inspection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Southeast Asia</td>
<td>Indonesia*</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Malaysia*</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cambodia*</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Philippines</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Brunei Darussalam</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Myanmar*</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>India*</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Bangladesh*</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Sri Lanka*</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Nepal</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Pakistan</td>
<td>4</td>
<td>8</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Central Asia</td>
<td>Uzbekistan*</td>
<td>16</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Kyrgyz Republic</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Armenia*</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kazakhstan*</td>
<td>10</td>
<td>10</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Afghanistan</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Georgia</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Azerbaijan</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Tajikistan</td>
<td>14</td>
<td>14</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pacific</td>
<td>Papua New Guinea</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

* Vaccine manufacturing site.

and customs clearance lead times between countries in three subregions shows that Oceania had the shortest times (Central Asia in Figure 8.6, South Asia in Figure 8.7, and Oceania in Figure 8.8).

**Figure 8.6: Import-Export Lead Time and Clearance Time in Countries in Central Asia**

Source: Author’s illustration, based on World Bank’s Logistics Performance Index (LPI). https://lpi.worldbank.org/domestic

**Figure 8.7: Import-Export Lead Time and Clearance Time in Countries in South Asia**

Source: Author’s illustration, based on World Bank’s Logistics Performance Index (LPI). https://lpi.worldbank.org/domestic
8.4.3 Best Practices for COVID-19 Vaccine Cross-Border Processes

When it comes to COVID-19 vaccines, most countries give high priority to cross-border processes as all governments wanted to obtain the vaccines as soon as possible. Therefore, import–export frameworks and procedures were modified or authorized to reduce import and export lead times for vaccines. Asia-Pacific Economic Cooperation (2021) provides best practices for customs administration in the region to facilitate the distribution of COVID-19 vaccines and related goods. Selected best practices guidelines relevant to cross-border and international logistics include the following:

- **Engagement with relevant traders:** Governments should collaborate with traders in the vaccine supply chains, including relevant businesses, health authorities, customs agency, industry stakeholders and logistics service providers, to ensure that all stakeholders are committed to working with the government to facilitate the movement of COVID-19 vaccines and related goods while maintaining cold chain practices and standards. Moreover, a 24-hour contact point for importers, exporters, and logistics service providers should be available to facilitate
shipments, respond to unexpected delays, and provide advice on any requests to avoid unnecessary delays.

- **Accelerated border clearance for COVID-19 vaccines and related goods:** Customs import clearance processes should be conducted prior to the arrival of COVID-19 vaccines and related goods as well as hazardous substances such as dry ice used to transport these vaccines to ensure import processes are as speedy as possible without unnecessary delay.

- **Border officers:** They should have a clear understanding concerning the logistics arrangements, such as approval and licensing processes and related documents, as well as issues to preserve the quality of COVID-19 vaccines and related goods during cross-border processes.

- **Digitalized process:** Customs export and import procedures should be conducted using digitalized trade documents and electronic payment to achieve the timely clearance and movement of COVID-19 vaccines and related goods.

- **Measures concerning counterfeits and unlawful movement of COVID-19 vaccines and related goods:** Appropriate measures such as verification processes should be implemented to detect substandard and/or counterfeit vaccines, for example, by including manufacture marks of authenticity and supporting documents.

- **Transparency:** The cross-border facilitation process of COVID-19 vaccines and related goods should be clearly communicated to importers, exporters, and relevant parties such as logistics providers as transparency is crucial for effective collaboration between customs administrations in the region.

- **Physical infrastructure:** Adequate facilities and infrastructure at the border are necessary to handle time- and temperature-sensitive COVID-19 vaccines and related goods.

The following are intervention measures implemented to smooth vaccine flows in several countries and selected best practices based on the above criteria:

- **Australia:** The Australian Border Force (ABF) established the Joint Planning Group (JPG), a committee comprising senior government officials and experts from businesses, to integrate cross-border agencies dealing with COVID-19 commodities to speed up the cross-border procedures while using security and safety measures to detect unlawful importation of vaccines. The JPG explored measures to support the flow of COVID-19 commodities across borders. Customs, biosecurity, and
health-related permissions were merged, and obstacles were removed to smooth cross-border procedures without unnecessary interruption or delay. The JPG displayed a strong collaboration between government and business to arrange the delivery of vaccine-related commodities and the movement of vaccines along the COVID-19 vaccine chains. Australia’s Therapeutic Goods Administration and Department of Health engaged pharmaceutical manufacturers and importers, with the ABF and the then Department of Agriculture, Water and the Environment sharing information on import requirements at the port or border level. A high level of collaboration between government and industry has resulted in delivery schedules and awareness of all stakeholders on vaccine movements. Moreover, Australia’s Department of Health and the World Customs Organization entered into a collaboration to conduct training courses at operational locations to ease cross-border procedures for critical COVID-19 commodities. In addition, the ABF also developed a risk assessment process through the JPG to manage ongoing risk mitigation.

The ABF’s goal has been to expedite cross-border procedures for COVID-19 vaccines. The targets have been 2 hours for cross-border lead time of COVID-19 vaccines that need to be stored in a cold room and 24 hours for other related items that can be kept in an ambient environment (WOC 2021).

- **India:** Inspecting and clearing COVID-19 vaccines for export and import to ensure the safety and security of the vaccines in India is under the supervision of the Central Board of Indirect Taxes and Customs and the Central Drugs Standard Control Organization (CDSCO). In addition, the Indian Customs Administration has also implemented an automatic risk management system to provide principles of risk-based management for conducting inspection and testing by the relevant government agencies such as CDSCO. The risk criteria of CDSCO are also integrated with the customs administration’s risk management system.

A COVID-19 Vaccine Response Team (CVRT) has been established at five air cargo terminals. The team comprises customs officers at the level of assistant or deputy commissioner, officers from the concerned logistics service providers, representatives from the Customs Brokers Association, and
officers from concerned partner government agencies. CVRTs are the single point of contact for all the clearance processes related to vaccine shipments. They closely collaborate with importers and exporters for instant clearance processes.

An electronic single window has been established by the Indian Customs Administration to integrate and share data between the customs department and other related government agencies such as CDSCO. The joint secretary, the customs department, is the focal entity to expedite the cross-border lead time of COVID-19-related items at the national level. For operational matters, officials at ports of entry are assigned to support customs clearance procedures. Their contact information is available on the Indian Customs Administration’s website, as well as a dedicated help desk consisting of a toll-free hotline and an email address. Documents required for cross-border processes are allowed to be submitted to the electronic single window about 24 hours prior to the arrival of the vaccines, so an advance assessment can be conducted. CRVTs are incorporated to conduct instant clearance and release of the vaccines at the port of entry. As a result, COVID-19 vaccines and related items can pass cross-border procedures within half an hour (WOC 2021).

- Indonesia: The Indonesia Customs Agency, Indonesia National Single Window, the National Agency on Drugs and Food Control, and the Ministry of Health have worked together closely to establish and implement standard operating procedures for cross-border COVID-19 vaccine operations. This collaboration supports the incoming flow of COVID-19 vaccines as well as the risk control measures. The Indonesia National Single Window agency provides an integrated import permit application, while Indonesia Customs organizes the customs clearance processes such as document and physical inspection (WOC 2021).

The customs clearance process is also supported by an immediate release facility, which allows importers to submit the import declaration document within 3 working days after the goods are released. To facilitate this process, the customs department, related government agencies, and importers work together closely to ensure that products and documents are in compliance.
The lead time to import COVID-19 vaccines is about 2 hours under the immediate release facility when the completed document is submitted, but the pre- and post-clearance lead times are excluded (WOC 2021).

- **Singapore**: Singapore Customs has created a strong collaboration between border agencies, related regulatory bodies, the health authority, and the private sector to support the importation and distribution of COVID-19 vaccines. The health authority provides guidance to the country’s border agencies on control protocols for the COVID-19 vaccines that facilitate the identification of shipments via the product code, product description, and the product interim authorization reference number declared in the permit declarations, as well as the vaccine properties. Border officers are trained to ensure that the integrity of the vaccines can be maintained during the customs clearance process. Moreover, border officers carry out work to reduce physical inspections for COVID-19 vaccine shipments while maintaining the integrity of Singapore’s border and supply chain security. The Singapore National Single Window that integrates and shares information with all related partners is used to process cross-border procedures starting from pre-arrival to the release of goods. Risk management is developed on the cross-border clearance process. Then, the permit declarations are assessed for risk and preapproved prior to the arrival of the COVID-19 vaccine shipments. These shipments can be released instantly upon their arrival if there is no warning from the risk assessment (WOC 2021).

- **Thailand**: From our in-depth interviews with GPO who is the only authorized importer of COVID-19 vaccines in Thailand, major pharmaceutical distributors who act as logistics service providers, the customs department at Suvarnabhumi international airport, and FDA officials; the Ministry of Public Health has established a joint working group including FDA, GPO, the customs border agency, and logistics service providers to plan and manage the importation of COVID-19 vaccines. The purchasing plans and delivery schedules are shared. The Thai national single window is used as a major tool to facilitate and accelerate the cross-border process. The required documents can be submitted through the single window system prior to the arrival of the COVID-19 vaccine shipments. The documentation inspection is conducted prior to the arrival of the shipments to maintain the integrity of the COVID-19 vaccines. If there is no
warning on the documents, the shipments can be released upon the arrival of the shipments. Only trusted and experienced logistics service providers are selected to manage the logistics flow of the COVID-19 vaccines from import to distribution across the country.

As a result of the strong collaboration among relevant stakeholders, the clearance process lead time can be shortened to less than 3 hours. Only value-added tax is applied for COVID-19 vaccines.

The customs clearance lead times for COVID-19 vaccines for selected countries are shown in Table 8.4.

<table>
<thead>
<tr>
<th>Country</th>
<th>Customs Clearance Lead Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>2 hours</td>
</tr>
<tr>
<td>India</td>
<td>30 mins</td>
</tr>
<tr>
<td>Indonesia</td>
<td>2 hours*</td>
</tr>
<tr>
<td>Thailand</td>
<td>Less than 3 hours</td>
</tr>
</tbody>
</table>

COVID-19 = coronavirus disease.

* If all required documents are provided, excluding pre- and post-clearance lead time.

Sources: World Customs Organization (2021) and in-depth interviews.

Major components contribute to the nature of good practices found in those selected countries include the following:

- Strong collaboration with government agencies, health authorities, logistics service providers, importers, exporters, and related stakeholders.
- A simplified work procedure of cross-border processes allows starting the clearance process prior to the arrival of the COVID-19 vaccines using the electronic documents provided by the national single window. Risk assessment applications are arranged to reduce physical inspections to maintain the integrity of the COVID-19 vaccines and the integrity of the border as well.
Relevant officers are trained to conduct their work properly so as to preserve the quality of the vaccines and prevent counterfeits and unlawful movements of COVID-19 vaccines and related products.

8.5 Challenges and Recommendations

8.5.1 Major Challenges

Through reviews and analysis of documents, guidelines, links, and online available resources, as well as in-depth interviews with key stakeholders in the COVID-19 vaccine cold chains, we have identified the following major challenges in international transport and cross-border trade and how to address them:

- The cold chain infrastructure is inadequate. Capacity is lacking for traditional, frozen, and ultra-cold chains, particularly in low- and lower middle-income countries in the Pacific and Central Asia. In some countries such as the Lao People’s Democratic Republic, Pakistan, and the Philippines, backup power sources, proper cold chain monitoring, and equipment maintenance may be insufficient.

- Requirements and procedures differ in terms of temperature management and control for different types of COVID-19 vaccines during cross-border transport. Moreover, different procedures are needed for handling passive and active cold boxes. These could lead to improper handling of vaccines during cross-border transport, resulting in vaccine inefficacy or wastage. Moreover, the major causes are found to be poor temperature management, low levels of technology; and insufficient skills, knowledge, and management capacity (ADB 2021).

- It is difficult to implement vaccine and temperature tracking and tracing systems, as well as data sharing among parties in vaccine cold chains to create supply chain visibility and temperature monitoring. Obstacles include insufficient budgets and technology, and the data management silos of parties in the supply chain.

- Seamless collaboration between importers and customs clearance agencies, and among logistics service providers, the health authority, and FDA is difficult to achieve.

- International transportation capacity differs between countries, and volatile freight capacity is limited. Moreover, since there are no direct flights from manufacturing countries to most
of the importing countries in the region, vaccine cargos need to go through at least one connecting flight. This could cause delays and pose more temperature excursion risk to the cold chain, especially in low-income countries in the region where cold chain airport facilities are limited. Based on our in-depth interview, one of the logistics service providers of the Pfizer–BioNTech vaccine pointed out that obtaining a direct and reliable flight schedule, including a transit flight, with total travel time of less than 72 hours was challenging during the global lockdowns. At the same time, the quality of the airport terminal, including temporary cold storage, has been a main consideration in selecting a flight.

• There is a lack of priority “green channels” and coordinated fast-track for vaccine inputs during cross-border trade. Additionally, the Pacific is behind other subregions with a 40.1% implementation rate of general and digital trade facilitation measures. Low capability to handle cross-border trade can affect cost, time, response to counterfeit goods, and quality of products traded across borders. This poses challenges in Central Asia and South Asia where manufacturing sites are in low-income countries such as Bangladesh, India, Sri Lanka, and Uzbekistan.

• Country-wide personnel training can help build supply chain flexibility in correctly handling different cold chains. Some types of refrigerants, such as dry ice, are defined as dangerous goods. The packing or loading operators must ensure that vaccine shipments are maintained at the required temperature without exceeding the limit for a particular aircraft type.

• Cultural resistance to vaccination translates into low participation in national programs (Nair et al. 2022).

8.5.2 Recommendations

Based on challenges in international, cross-border transport, we present six key recommendation areas to improve vaccine transport connectivity and to better prepare for the next pandemic. The key findings and recommendations are also shown in Figure 8.9:

(i) Cross-border policy and regulations: Harmonized policies and regulations among partner countries, including sharing information and effective collaboration, are needed. Implement relevant measures to facilitate and secure cross-border movement, coordinate with other government agencies and stakeholders, and prioritize and facilitate
clearance and control risks. Additionally, develop standard operating procedures for import and export of COVID-19 vaccines, vaccine inputs, and related supplies and equipment. Both physical and cyber security measures must be in place to protect vaccines against theft and counterfeiting.

(ii) **Cold chain logistics, infrastructure, and readiness:** Governments need to ensure the readiness of cold chain equipment and facilities and conduct a capacity assessment. Conduct advanced vaccine distribution planning for estimates of space requirements in each temperature range. If possible, implement pharmaceutical grade refrigerator or cold room procurement. More importantly, countries in the region should work together to improve cold chain logistics planning and request that donor countries and organizations contribute cold chain equipment and facilities as soon as possible.

(iii) **Readiness of human resources to handle vaccine cold chain:** Offer human resources training and an easy-to-understand procedure manual in local languages to ensure compliance. Knowledge sharing among member countries and e-learning are helpful as well. Customs officers should have a better understanding of cold chain requirements and integrity to authorize paperwork in a timely manner.

(iv) **Cooperation and coordination:** Establish a national working group and announce and implement a government policy for cooperation and coordination among private and government organizations regarding cross-border transport and logistics. Identify key stakeholders to ensure smooth, timely, and effective cross-border trade processes. Furthermore, designate government officials as key contact points for cross-border procedures. Additionally, assign officials to be on duty 24–7 to ensure cross-border logistics are processed swiftly. Synchronization and collaboration between customs, health authorities, importers, and logistics service providers with timely regulatory approvals, inspection, and clearance are crucial (IATA 2021). Then, strong collaboration between vaccine manufacturers, importers, third-party logistics providers, and customs clearance is necessary to ensure accurate details of vaccines, flight, arrival time, and other relevant information so that appropriate customs clearance processes, truck booking, cold room reservation, and other facilities or activities can be arranged. During the transport of vaccines, adequate security measures must be in place to ensure shipment from counterfeiting and theft, such as real-
time monitoring of temperature and status of COVID-19 vaccines.

(v) **Professional health-care logistics service providers**: Work with professionals and experts in pharmaceutical logistics. It might cost more to work with experts and professionals, but they are more reliable, and vaccine efficacy would be affected if cold chain integrity is violated. In Thailand, there are two main well-known logistics service providers handling COVID-19 vaccines. One works with traditional cold chain vaccines and the other with frozen and ultra-cold vaccines. They both increased their cold chain capacities and won logistics contracts from the government.

(vi) **Information technology readiness and cold chain visibility**: Develop a national cold chain tracking and tracing system to ensure information sharing and the monitoring of cold chain integrity.
**Figure 8.9: Key Findings, Recommendations, and Stakeholder Mapping**

### Procedure and human resources
- Difficulty in seamless collaboration among relevant parties
- Key contact point should be assigned to ensure 24-7 availability
- Different cold chains with different handling requirements and procedures
- Vaccine quality and efficacy assurance
- Countrywide personnel training to build flexibility in correctly handling different cold chains

### Regulations and cold chain infrastructure
- Limited and volatile freight capacity
- Readiness of cold chain transport truck with temperature monitoring
- Lack of priority “green channels” and coordinated fast track for vaccine inputs during cross-border transport
- Inadequate cold chain infrastructure
- Vaccine and temperature tracking and tracing system
- Temperature reports and package seals

### Major challenges
- Cooperation and coordination: Key stakeholders must be identified to ensure a smooth, timely, and effective process of cross-border transport.
- Cross-border policy and regulations: Harmonized policies and regulations among country partners are needed, including information sharing and effective collaboration, as well as implementation of relevant measures used to facilitate and secure cross-border movement.
- Cold chain logistics, infrastructure, and readiness: Complete cold chain readiness must be in place, along with training and compliance. Member countries in the region work together to improve cold chain assessment and capability.
- Develop national cold chain tracking and tracing system
- Easy-to-understand training of human resources

### Key success factors
- Working group among the key stakeholders from government agencies and the private sector
- Vaccine manufacturers and inputs suppliers
- Logistics service providers
- Government agencies, e.g., FDA, department of disease control, and customs.

### Stakeholder mapping
- Working group among the key stakeholders from government agencies and the private sector
- FDA at port of entry, customs administrator, and security measures controllers
- Ministry of health
- Logistics service provider and warehouse operators
- Airport terminal staff

FDA = Food and Drug Administration.

Sources: Asian Development Bank (2021), International Air Transport Association (2021), World Customs Organization (2021), and in-depth interviews.
References


PART III

Regulatory Cooperation and Accessibility of Vaccines
9

Trade, Investment, and Cooperation in the Health Sector and Vaccines in Asia and the Pacific

Arpita Mukherjee and Eshana Mukherjee

9.1 Introduction

Comprising more than 50 countries, Asia and the Pacific is the largest region in the world, in terms of area and has the world’s most populous countries such as the People’s Republic of China (PRC) and India. The region, with several developing countries and least-developed countries (LDCs), was one of the fastest-growing regions in the world prior to the coronavirus disease (COVID-19) pandemic. Despite the economic slowdown due to the pandemic, the International Monetary Fund predicted that there will be a strong rebound for the region and projected that it will remain one of the fastest-growing regions in the world with 4.2% growth in 2023 (IMF 2022). However, the growth and post-COVID-19 recovery remain unbalanced because of repeated pandemic breakouts and varying health-care needs, which have put a strain on government budgets. With over 60% of the world population living in Asia by 2030, one in four over the age of 60 years, and a compound annual growth rate of 10% in developing countries, health care is a crucial sector in this region (APACMed and Deloitte 2020; Goldstein Market Intelligence 2019).

1 For the full list of countries, please refer to Economic and Social Commission for Asia and the Pacific (ESCAP) web page at https://www.unescap.org/about/member-states.

2 As of September 2022, the PRC’s estimated population is 1.42 billion and India’s population 1.41 billion. For more details, see World Population Review website at https://worldpopulationreview.com/.
As the health-care sector continues to grow, trade in health products has also increased, and the need to facilitate trade was further accelerated during the pandemic. According to the World Trade Organization (WTO), exports of medical products were valued at $957.7 billion in 2018, which increased to $1,159.7 billion in 2020. With the advent of the COVID-19 pandemic in the second half (S2) of 2019, medical products accounted for 5.4% of total world merchandise trade; by the first half (S1) of 2021, the share increased to 6.1% (WTO 2021). As the pandemic progressed over the months, however, it also led to severe shortages of key medicines and medical devices in many countries; over 90% of countries faced sudden disruptions in supply chains, and there has been growing trade protectionism. The COVID-19 pandemic thus also highlighted the need for greater trade, investment, and cooperation in Asia and the Pacific, as countries seek to recover from the pandemic and build back better.

Historically, trade, cross-border investment, and cooperation have been powerful drivers to help countries address insufficient and unequal access to essential health products and services. Commitments under trade agreements help to secure the free flow of goods, investments, and services, and collaboration and cooperation can help address issues related to unequal access to health care (ADB 2019). In light of the supply chain and trade disruption subsequent to the pandemic, countries in the Asia and the Pacific have signed several trade agreements since 2020 and are now exploring ways and means to use measures like mutual recognition of vaccines to facilitate trade. One example of a mega regional agreement is the Regional Comprehensive Economic Partnership (RCEP) Agreement, signed by 15 countries, which can help to synergize the rules of origin and mitigate some of the negative effects of the pandemic related to supply chain uncertainties (Thangavelu, Urata, and Narjoko 2021). Regional blocs such as the Association of Southeast Asian Nations (ASEAN) took measures to mitigate supply chain disruptions. In 2020, ASEAN member countries got together to adopt the Hanoi Plan of Action to strengthen economic cooperation in supply chain connectivity to ensure a smooth flow of essential goods and prevent further supply chain disruptions (ASEAN 2020).

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3 RCEP is a free trade agreement between the 10 ASEAN member states (Brunei Darussalam, Cambodia, Indonesia, the Lao People’s Democratic Republic, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Viet Nam) and its five free trade agreement partners (Australia, Japan, New Zealand, the PRC, and the Republic of Korea) signed on 15 November 2020. For more details, see the RCEP website at https://rcepsec.org/.
The health-care sector receives budgetary support from governments in most countries, in the form of subsidies, reduced taxes, and/or grants to meet universal service obligations and to attract private investment. For instance, subsidies are given to boost the production of medical supplies\(^4\) or to reduce the cost of vaccines to enhance their access.\(^5\) The pandemic further created the need for increased private investments. Such investments are required, not only in delivery of core services like hospitals, clinics, laboratories, and education for medical professionals, but also in research for drugs and vaccines, vaccine administration training, clinical trials, ancillary services like insurance and ambulance services, and health-care support in distribution, data collection, collation, and analytics.

In this context, this chapter discusses the importance of trade, investment, and cooperation in the health sector and vaccines with an objective of addressing the pandemic and future health disasters. It highlights the scope, coverage, and extent of commitments in the health-care sector in trade agreements, and the potential for using trade agreements and other cooperation channels to improve access to health care, with a focus on vaccines and essential health products. It is based on secondary information and data analysis, as well as 25 key informant interviews covering different stakeholders including the private sector, nongovernment organizations and foundations, international organizations, academic experts, and policymakers.

Section 9.2 presents an overview of trade, investment, and collaborations and initiatives in the health-care sector in Asia and the Pacific in the context of COVID-19 and related essential health and medical goods. Section 9.3 focuses on the trade agreements signed pre- and post-COVID-19, highlighting the gaps and barriers. Section 9.4 presents the way forward and recommendations for better coverage of the health sector in trade agreements and improved collaborations among industry stakeholders.

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\(^{4}\) For example, Tamil Nadu, India, offers a capital subsidy of 30% for fixed assets and waives the requirement for authorization or clearance from local authorities to increase the production of medical supplies and machinery used in the COVID-19 response (UNCTAD 2020a).

\(^{5}\) For example, the Government of India with liberalized vaccine pricing, incentivized vaccine manufacturers to scale up production, attracted new manufacturers, and ensured wider availability of vaccines across the country. For more details, see Ministry of Health and Family Welfare (2021).
9.2 Trade, Investment, and Cooperation for COVID-19 Health-Care Products in Asia and the Pacific

The global market for medical products is projected to grow at an average annual rate of 22.9% from 2019 to 2023, rising from 14.60 billion units to over 33.36 billion units over this period. Among the four main groups of medical products—medical equipment, medical supplies, medicines, and personal protective products—medicines accounted for more than 50% of trade in medical products (WTO 2021). Some of the top countries exporting COVID-19 critical health-care products are in Asia and the Pacific.

9.2.1 Trade in COVID-19 Health-Care Goods and Vaccines

The global demand for medical products varies at the different stages of the pandemic. In the beginning of the pandemic, the demand for ventilators, personal protective equipment (PPE) kits, testing kits, and drugs peaked. For example, in the second half of 2020, the demand for ventilators doubled in trade value with a year-on-year growth of 95.3% (WTO 2021). The spike in demand has since then flattened, because such medical equipment is both durable and reusable and is generally linked to hospital capacity. Also, because of the sudden increase in demand and export restrictions, countries previously dependent on imports for COVID-19-related products started producing ventilators to mitigate the fear of supply chain disruptions. With the number of COVID-19 cases reducing, the exports of ventilators and face masks slowed. Following the development and approval of COVID-19 vaccines, cross-border trade in items critical for administering vaccines such as rubber gloves, syringes, and needles has grown (WTO 2021). In the first quarter of 2020, rubber gloves, syringes, and needles accounted for only 10% of trade in medical supplies, but the share almost doubled to more than 18% by the second quarter of 2021.

Countries like India, which have enhanced their domestic manufacturing capabilities in specific products, have seen a growth in exports (Box 9.1).
Box 9.1: India—A New Production Hub for Personal Protective Equipment Kits and Vaccines

With a surge in demand for personal protective equipment (PPE) kits globally, the Ministry of Textiles, Ministry of Health and Family Welfare, and domestic textile companies in India were quick to collaborate and made India a PPE manufacturing hub (Nayyar and Lakshmanan 2020). In 2019, India’s exports of products under the Harmonized System (HS) Code 621010, which covers protective garments for surgical and/or medical use like coveralls, were worth about $6.5 million and imports worth $5.7 million. In 2020, exports increased to $82.5 million and imports to $35.8 million.

India is one of the leading vaccine manufacturing hubs globally. The exports of vaccines (HS Code 300220) increased from $772 million in 2019 to $1,107 million in 2021. The significant increase in exports can be attributed to exports of coronavirus disease (COVID-19) vaccines. The Made in India COVID-19 vaccines have also been a key part of the country’s geostrategic diplomacy. India provided vaccines to least-developed countries in the Association of Southeast Asian Nations region and Africa, for example.

As of November 2022, India was the largest vaccine producer and the second-largest country to export PPE kits to the world.

Sources: Compiled from various sources, including Nayyar and Lakshmanan (2020); UN Comtrade database https://comtrade.un.org/data/; The Times of India (2022); and Invest India web page at https://www.investindia.gov.in/sector/pharmaceuticals.

Malaysia has been the largest supplier of rubber gloves with a share of more than 50% of the global market, even before the COVID-19 pandemic. The other top suppliers of rubber gloves are the PRC, Thailand, and Indonesia, ranking second to fourth, respectively (WTO 2021). Thus, most suppliers of rubber gloves are in Asia, which accounts for 86% of the export market for gloves. In Asia and the Pacific, the PRC (1st), Malaysia (5th), and Japan (6th) have been the major exporters of COVID-19 critical health products since 2020. Overall, there has been a rise in trade in health-care products, but demand within this sector for different products is changing over time.

Focusing on trade of COVID-19 vaccines, as of 31 May 2022, approximately 6.2 billion doses have been traded. Of the total supply, Asian countries such as the PRC (32.2%), the Republic of Korea (3.9%), and India (2.3%) are among the top exporters (WTO and IMF 2022). Countries have supplied vaccines through various arrangements like contracted supply via the COVID-19 Vaccines Global Access (COVAX), direct donations, domestic supply, or bilateral deals. For example,
Table 9.1: Trade Value in Medical Products with a Focus on COVID-19-Related Products ($ billion)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All medical products</td>
<td>999.60</td>
<td>1,162.231</td>
<td>1,320.46</td>
<td>1,028.23</td>
<td>1,197.54</td>
<td>1,333.28</td>
</tr>
<tr>
<td>Medical equipment</td>
<td>140.90</td>
<td>151.05</td>
<td>162.81</td>
<td>145.11</td>
<td>157.58</td>
<td>166.42</td>
</tr>
<tr>
<td>Ventilators</td>
<td>8.03</td>
<td>14.03</td>
<td>11.26</td>
<td>8.35</td>
<td>15.48</td>
<td>12.19</td>
</tr>
<tr>
<td>Medical supplies</td>
<td>172.78</td>
<td>204.97</td>
<td>238.15</td>
<td>172.28</td>
<td>204.62</td>
<td>247.78</td>
</tr>
<tr>
<td>Test kits and diagnostic reagents</td>
<td>28.14</td>
<td>39.57</td>
<td>46.62</td>
<td>28.80</td>
<td>42.00</td>
<td>58.20</td>
</tr>
<tr>
<td>Rubber gloves</td>
<td>7.95</td>
<td>16.69</td>
<td>26.28</td>
<td>8.40</td>
<td>16.00</td>
<td>29.37</td>
</tr>
<tr>
<td>Syringes and needles</td>
<td>8.70</td>
<td>8.86</td>
<td>10.38</td>
<td>9.37</td>
<td>9.51</td>
<td>11.45</td>
</tr>
<tr>
<td>Medicine</td>
<td>546.24</td>
<td>604.37</td>
<td>738.24</td>
<td>572.32</td>
<td>625.73</td>
<td>741.88</td>
</tr>
<tr>
<td>Personal protective products</td>
<td>139.68</td>
<td>201.92</td>
<td>181.26</td>
<td>138.50</td>
<td>209.60</td>
<td>177.19</td>
</tr>
<tr>
<td>Face masks</td>
<td>77.30</td>
<td>137.10</td>
<td>106.19</td>
<td>78.68</td>
<td>143.57</td>
<td>102.21</td>
</tr>
<tr>
<td>COVID-19 critical products</td>
<td>304.184</td>
<td>395.89</td>
<td>393.32</td>
<td>305.021</td>
<td>405.21</td>
<td>393.79</td>
</tr>
</tbody>
</table>

Note: Critical medical products include disinfectants or sterilization products, face masks, gloves, hand soap and hand sanitizer, patient monitors and pulse oximeters, protective spectacles and visors, sterilizers, syringes, thermometers, ultrasonic scanning apparatus, ventilators, oxygen masks, X-ray equipment, and other devices such as computer tomography apparatus.


Australia has donated 1,725,750 doses of the Pfizer–BioNTech vaccine to the Philippines, as of February 2022 (Center for Strategic and International Studies 2022). Another example is the Quad Vaccine Partnership, whereby Cambodia received over 3,000 COVID-19 vaccine doses. Bilateral deals and strategic alliances have helped to facilitate a faster and smoother cross-border movement of vaccines, vaccine inputs, and related supplies (Box 9.2).

However, despite the COVID-19 emergency and urgent requirement of critical products needed to administer the vaccines, high tariffs were an impediment to smoother cross-border movement of critical products. For example, the average applied most-favored-nation tariffs on rubber gloves by WTO members was 8.2% in 2021. There are also issues related to recognition of vaccines developed in other countries, which delayed vaccine administration.
9.2.2 Trade in Services

As countries closed their borders, restricted visas, and enforced quarantines, cross-border mobility of people suffered. It resulted in a severe shortage of health-care workers, with many developed countries open to attracting health-care professionals and workers from developing countries to manage their needs, leading to possibilities for short-term movement of health-care professionals such as doctors and nurses from developing countries like India (Veeramani and Anam 2021). Developed countries such as the United States (US), the United Kingdom (UK), and Australia relaxed their work permit and visa rules as measures to meet the shortages in the sector (Press Trust of India 2020). However, the developing countries and LDCs are facing the maximum shortages of health-care workers to administer the vaccine, creating a need for cross-border mobility of health-care workers.

Services backed by digital technologies such as teleworking and telemedicine have emerged as the key drivers of a new globalism during the pandemic (Lashitew and Erumban 2020; Marel and Guinea 2020). The number of users of online medical platforms in countries in Asia and the Pacific such as Australia, Indonesia, the PRC, and Singapore have grown rapidly during the pandemic. The pandemic has also created a need for remote access to doctors and other support, leading to the development of digital therapy apps, online doctor consultation apps, and other apps, many of these being designed by start-ups in the region. For research and development of vaccines and monitoring of its impact, cross-border sharing of data and information and joint clinical trials are necessary. Cross-country collaborative research has emerged in this field. For example, the Pfizer vaccine was created by Turkish immigrants working in Germany’s BioNTech SE, and the AstraZeneca vaccine by researchers at the University of Oxford in the UK and

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**Box 9.2: COVID-19 Vaccine Supply in Asia**

Asia received a total of 9,811.3 million doses through various arrangements like contracted supply via COVAX, direct donations, or domestic supply. While domestic supply accounts for 66.6% share in the total supply, 24.4% doses were supplied via bilateral deals. In Asia, the People’s Republic of China and India were the top vaccine suppliers, supplying approximately 13% of the vaccines through bilateral deals.

produced by the Serum Institute of India (SII) in India (Bown and Bollyky 2021).

9.2.3 Cross-Border Investments

Cross-border investments in the health-care sector have for the most part included developed countries investing in developing countries or LDCs. The sector receives investment in manufacturing of medical goods and medicines, in pharmaceutical products where companies sometimes allow transfer of technology, in research and development (R&D), or in the form of infrastructure (like hospital buildings and clinics). In 2019, the health sector in developing Asia attracted foreign direct investment (FDI) totaling $3,693 million in greenfield projects and project financing. This declined to $2,464 million in the pandemic year 2020. Singapore observed a decline by 20.7% in their FDI inflows in 2020 and Uzbekistan by 26% (UNCTAD 2021). On the other hand, countries like the PRC and India observed increased inflows in 2020. These two countries are two of the largest COVID-19 vaccine producers and suppliers (Box 9.2).

Cross-border investment allowed for better allocation of resources to R&D and manufacturing to countries with the capability to mass-produce COVID-19 vaccines in a short period of time. It also enabled transfer of technology and development of new global supply chains for manufacturing COVID-19 vaccines (UNCTAD 2020a; Bown and Bollyky 2021). As mentioned in section 9.2.2., while the AstraZeneca vaccine was developed by researchers in the UK, it outsourced the manufacturing, transferring the required technology to other countries such as India, Thailand, Japan, and Australia. The largest AstraZeneca manufacturer is SII (Bown and Bollyky 2021).

9.2.4 Initiatives and Collaborations to Tackle COVID-19

With a rise in shortage of key medicines, health-care workers, and medical devices across Asia and the Pacific due to sudden export bans and lockdowns, international organizations such as the World Health Organization (WHO) and the WTO emphasized the need for cooperation, especially at the regional level to reduce supply chain and logistics disruptions as well as to improve the production capacity for vaccines and other medical products (Mukherjee, Mukherjee, and Goswami 2022). This led to various kinds of collaborations across multiple stakeholders in manufacturing and R&D, stronger and more efficient supply chain logistics, online and fast-track clearances by
customs and drug regulators, and easier mobility of health-care workers, at both country level and through international and regional organizations (UNCTAD 2020a; Mukherjee, Mukherjee, and Goswami 2022). Some examples are illustrated in Box 9.3.

**Box 9.3: Increasing Access to COVID-19 Vaccine in Asia and the Pacific—Some Examples**

- In April 2020, to tackle coronavirus disease (COVID-19), the Asian Development Bank (ADB) committed a $20 billion package in a mix of loans, grants, technical assurance, and debt security for identified projects across countries and regions in Central and West Asia, East Asia, South Asia, Southeast Asia, and the Pacific that included a $9 billion vaccination package.
- In May 2021, the Association of Southeast Asian Nations (ASEAN) and the European Union held a dialogue on vaccine security to engage medical specialists, policy practitioners, and industry representatives from BioNTech to strengthen cooperation and efforts of making COVID-19 vaccine accessible to all through knowledge sharing and capacity building.
- In 2022, the World Health Organization announced a collaboration with the Republic of Korea, opening a global biomanufacturing hub to provide training to low- and middle-income countries to help increase their vaccine production.
- In April 2022, under the Quadrilateral Security Dialogue, India, Australia, Japan, and the United States handed over 325,000 doses of Covishield vaccine to Cambodia as part of the Quad Vaccine Partnership. The initiative also aims to ensure vaccine availability of safe and effective vaccines by expanding manufacturing and helping countries in the Indo-Pacific region with vaccination.

Sources: Pharmaphorum (2022); ADB (2020); ASEAN (2021); and The Indian Express (2022).

Other developments during the pandemic include the liberalization of data-sharing policies for critical health-care data for research on drugs, vaccines, treatment, etc., including cross-border research, and monitoring the spread of the disease. Some examples of liberalization in policies to enable data sharing are given in Box 9.4.
From Lab to Jab: Improving Asia and the Pacific’s Readiness to Produce and Deliver Vaccines

The customs clearance process has been streamlined using technology, and many countries in the region have implemented a faster product approval process. To prevent further spread of COVID-19, without it disrupting logistics, supply chains, and trade flow of raw materials and inputs to produce the vaccine, easy access to information on trade procedures is important. Countries and organizations have thus developed online information portals to streamline the availability of necessary information and procedure. For example, the United Nations Conference on Trade and Development (UNCTAD) Automated System for Customs Data, implemented in more than 90 countries, provides customs personnel, cross-border agencies, and traders the ability to submit and exchange required documents and data electronically, expediting the clearance of imports and exports and reducing the need for face-to-face interaction (UNCTAD 2020b). In products like medicines and medical devices, the key informant interviews found that in countries like India, clearances by authorities like the Drug Controller are made online through implementation of a technology-based risk management system.

The next section analyzes the trade agreements in Asia and the Pacific, with a focus on COVID-19 vaccine.

Box 9.4: Examples of Liberalization in Data-Sharing Policies in the Pandemic

In April 2020, the Government of Singapore introduced a Bluetooth-based mobile application, which permitted users to receive a notification when they have been in close contact with individuals who have been infected by the virus (Abay, Tafere, and Woldemichael 2020). The data were shared with public health authorities to analyze and predict epidemic spread (WTO 2020).

In the Republic of Korea, prior to the coronavirus disease (COVID-19) pandemic, the Personal Information Protection Act (PIPA), 2011 banned collection, use, and disclosure of personal data without the prior informed consent of the concerned individuals. During COVID-19, amendments were made to the Contagious Disease Prevention and Control Act (CDPCA) of 2009, and authority was granted under CDPCA to override certain provisions of the PIPA and other privacy laws. It allowed sharing of seven categories of data, which included sensitive data such as geo-location data, personal identification information, prescriptions, and other medical records that pertain to infected individuals. The amendment allows the Korea Disease Control and Prevention Agency to share data with central, municipal, or local governments, national health insurance agencies, and health-care professionals and their associations (Park, Choi, and Ko 2020).
9.3 Bilateral and Regional Trade Agreements in Asia and the Pacific

Asia and the Pacific accounts for 48% of the total regional trade agreements and free trade agreements (FTAs) in the world. Some economies such as American Samoa, French Polynesia, Guam, and Timor-Leste do not have trade agreements, while others like Singapore have more than 20 trade agreements. Aside from a few countries, such as Bhutan, the Islamic Republic of Iran, and Palau, most countries in Asia and the Pacific are members of the WTO. These countries for the most part comply with the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and have commitments in areas like trade in goods and services, which to a certain extent facilitate trade in health-care products and services. They also abide by other WTO agreements such as the Technical Barriers to Trade (TBT) Agreement or the Sanitary and Phytosanitary Measures (SPS) Agreement.

The coverage and scope of the trade agreements in the region vary widely. For example, the WTO’s 1994 Agreement on Trade in Pharmaceutical Products covers a limited number of developed countries of the region. Other trade agreements vary in their coverage of goods and services, with some agreements covering only goods, some only services (e.g., European Union–Armenia FTA); some cover goods, services, and investment (South Asian Free Trade Area); and yet others are comprehensive new-age trade agreements, such as the Australia–New Zealand Closer Economic Relations Trade Agreement, India–Japan Comprehensive Economic Partnership Agreement (CEPA), and others, covering trade in goods, trade in services, investment, intellectual property rights government procurement, trade facilitation, and so on.

In terms of coverage of health-care products, it is overall limited. Some regional trade agreements, such as the Treaty on a Free Trade Area between members of the Commonwealth of Independent States and the Pacific Island Countries Trade Agreement, do not cover trade in health-care products. These mostly involve LDCs that need private and foreign investment to support government efforts to meet and/or enhance access to health-care goods and services.

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6 Compiled from the WTO Regional Trade Agreements Database.
7 Asia and the Pacific has 53 ESCAP members and 9 associate members located in five major subregions—East and North-East Asia, North Central Asia, the Pacific, South-East Asia, and South and South-West Asia (ESCAP 2019).
8 For more details, refer to the WTO Pharma Agreement web page at https://www.wto.org/english/tratop_e/pharma_ag_e/pharma_agreement_e.htm.
9.3.1 Analysis of Trade Agreements in Goods

This section focuses on how tariff and non-tariff issues like standards are addressed through trade agreements.

A. Tariffs

In Asia and the Pacific, while many countries have reduced autonomous tariffs for health products, tariffs continue to be high in some countries. Countries in the region such as Bangladesh (43.3%), India (40.5%), Maldives (32.9%), Nepal (21.4%), Pakistan (61%), and Thailand (24.7%) have high average bound duty on all medical products (WTO, ITC, and UNCTAD 2020). Along with basic customs duty, some countries like India have imposed a number of cess in recent years, increasing overall import costs. In some cases, tariffs are high on intermediate products compared to final products under the trade agreements, leading to an inverted duty structure. This prevents LDCs and developing countries from becoming manufacturing hubs of pharmaceutical products and medical devices. While trade agreements can facilitate trade, some COVID-19 health products are not covered. Trade agreements in this region vary by the size of their exclusion list and the period of tariff phaseout. Trade agreements such as the India–Japan CEPA and the ASEAN–Japan Economic Partnership Agreement, and the RCEP do not cover personal protective products such as hand sanitizers (HS code 38089400), disposable face masks (HS code 90192090), and medical or COVID-19 test kits (HS code 300215), essential during the pandemic. No ASEAN member state has committed to medical kits including COVID-19 kits (HS code 300211) in the RCEP. In the ASEAN Trade in Goods Agreement, some ASEAN countries have given liberal commitments to medical kits (HS 300211). For example, Brunei Darussalam, the Lao People’s Democratic Republic, Malaysia, Singapore, Thailand, and Viet Nam have had a 0% tariff for medical kits since 2017. In the RCEP, Australia, the PRC, Japan, the Republic of Korea, New Zealand, and Malaysia have not given commitment to masks (HS code 630790), whereas ASEAN countries such as Brunei Darussalam, Indonesia, the Philippines, and Viet Nam have committed to zero tariff for masks (HS code 630790) since the implementation of the agreement (1 January 2022).

B. An Analysis of Liberalization under Trade Agreements: Focusing on Necessary Goods for Vaccination in Trade Agreements

Countries in Asia and the Pacific have liberalized tariff on goods necessary for vaccination drives, such as needles and syringes, rubber gloves, and similar equipment, in their trade agreements (Table 9.2),
Table 9.2: Examples of Vaccination Products
Liberalized under Various Trade Agreements

<table>
<thead>
<tr>
<th>Trade Agreement/ Countries</th>
<th>Products and HS Codes</th>
<th>Tariff Liberalization Commitment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional Comprehensive Economic Partnership</td>
<td></td>
<td></td>
</tr>
<tr>
<td>People’s Republic of China, Japan, Republic of Korea, New Zealand, and ASEAN countries (Brunei Darussalam, Malaysia, Philippines, Thailand)</td>
<td>• Gloves (including rubber gloves) (HS code 401511 and 401519)  &lt;br&gt; • Needles and syringes (HS code 901832)</td>
<td>0% tariff at the time of implementation of the agreement (January 2022)</td>
</tr>
<tr>
<td>Australia</td>
<td>• Gloves (HS code 401511 and 401519)</td>
<td>Reduce tariff to 0% from 5% from the time of implementation</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>• Gloves (HS code 401511)</td>
<td>Reduce tariff to 0% from 20% year 10 onward</td>
</tr>
<tr>
<td>Lao People’s Democratic Republic and Myanmar</td>
<td>• Gloves (HS code 401511 and 401519)</td>
<td>Reduce tariff to 0% from 5% year 13 onward</td>
</tr>
<tr>
<td>Cambodia and Indonesia</td>
<td>• Gloves (HS code 401511 and 401519)</td>
<td>Reduce to 0% from 7% year 15 onward</td>
</tr>
<tr>
<td>ASEAN Trade in Goods Agreement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cambodia, Indonesia, Lao People’s Democratic Republic, and Viet Nam</td>
<td>• Gloves (HS code 401511 and 401519)</td>
<td>0% tariff since 2017</td>
</tr>
<tr>
<td>• Needles and syringes (HS code 901832)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASEAN–Australia–New Zealand Free Trade Agreement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>• Gloves (HS code 401511 and 401519)</td>
<td>Eliminated tariff to 0% since 2012</td>
</tr>
<tr>
<td>India–Japan Comprehensive Economic Partnership Agreement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>Under B10 category:  &lt;br&gt; • Gloves (HS code 401511 and 401519)  &lt;br&gt; • Needles and syringes (HS code 901832)</td>
<td>0% tariff since 1 January 2021</td>
</tr>
</tbody>
</table>

ASEAN = Association of Southeast Asian Nations, HS = Harmonized System.

Source: Compiled by the authors.
but the phaseout period in some agreements is long. The long phaseout reduces the benefits of tariff liberalization at the time of the pandemic.

C. Rules of Origin
Rigid rules of origin (ROO) can restrict trade. In the case of the pharmaceutical sector, the regional value addition is as high as 50% in certain agreements, as in the 2004 Japan–Mexico Agreement for the Strengthening of the Economic Partnership. Often, a very high percentage of value addition in the ROO acts against value chain development in health sector products. With the proliferation of trade agreements, multiple ROO and complexities in complying with them can add to trade costs, discouraging businesses from taking advantage of FTA privileges. The RCEP has tried to harmonize the ROO in the region and add more clarity.

D. Non-Tariff Measures: Technical Barriers to Trade and Sanitary and Phytosanitary Measures
Non-tariff measures (NTMs) under trade agreements cover issues such as approval process of drugs and vaccines, mutual recognition of standards and degrees of practitioners, and labeling requirements. To facilitate trade, chapters on the TBT Agreement and SPS measures can have provisions for harmonizing standards and preventing unnecessary NTMs (Mukherjee, Mukherjee, and Goswami 2022). At the same time, non-recognition and/or delays in approval have resulted in limited access to vaccines and related medical goods in the region (ADB 2022).

E. Trade Facilitation
Some of the more recent agreements, such as the India–United Arab Emirates CEPA, have tried to create a framework to fast-track clearances of health-care products to facilitate trade (e.g., Box 9.5).
9.3.2 Commitments in Health-Care Services

In Asia and the Pacific, countries and regional blocs have different approaches to commitments in their trade agreements. Asia’s largest agreement, the RCEP, follows a negative approach to service commitments and provides service suppliers information on the existing measures and regulations of RCEP member countries. The coverage of commitments in the health sector varies. For example, India and Japan in the India–Japan CEPA gave commitments in medical and dental services, services provided by midwives, nurses, etc., and hospital services, but there are also several restrictions. These include FDI being allowed only through incorporation with a foreign equity ceiling of 74%, subject to conditions in India. Australia has given commitments in other human health services such as chiropody services in the ASEAN-Australia-New Zealand FTA. Overall, there are multiple restrictions on cross-border mobility of health-care workers ranging from degree recognition to work permits and visa-related issues. There are also various restrictions and requirements on FDI. For example, in Myanmar, up to 70% foreign equity participation is permitted in accordance with the Law relating to “Private Health Care Services 2007” in medical and dental services and services provided by midwives. In India, in pharmaceutical production and R&D, restrictions are in place to ensure local investor participation.

Box 9.5: India–United Arab Emirates Agreement—Bilateral Cooperation on Pharmaceutical Products

The bilateral cooperation between India and the United Arab Emirates (UAE) on pharmaceutical products aimed to facilitate access to finished pharmaceutical products, and certain marketed biological products for human use by establishing “fast-track” procedures for approval of pharmaceutical products that have been approved by at least one national regulatory authority from Australia, Canada, the European Union, Japan, the United States, or the United Kingdom. It states that marketing authorization shall be provided within 90 days without any inspections if approved by the regulators of the listed countries in both markets but, for all other pharmaceutical products where inspections are required, India and the UAE, to the extent possible and feasible, will grant marketing authorization within 270 days of the application for such authorization.

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(UNCTAD 2021). These multiple restrictions and conditions led to a severe shortage of frontline workers and skilled health-care workers during the pandemic, when services of doctors and nurses were needed to treat COVID-19, as well as for mass vaccine administration (for details, refer to Mukherjee, Mukherjee, and Goswami 2022).

9.3.3 Mutual Recognition of Standards, Qualification, and Cooperation

Mutual recognition of standards for goods and qualifications and experience for services can be part of trade agreements or outside, through bilateral or regional arrangements in the form of mutual recognition agreements (MRAs) or memorandums of understanding (MOUs). For example, ASEAN members signed an MRA in 2003 allowing for free movement of health-care workers within the region. It focused on professional nursing services, their mobility, capacity building and training, and exchange of information and expertise of standards and qualifications. In June 2018, India and Singapore signed an MRA in nursing with Singapore agreeing to recognize seven more Indian nursing institutions. This has helped more Indian health-care service providers to institutionally access markets abroad (Press Information Bureau 2018). Several MRAs have been signed, but only a few have been implemented successfully in countries in Asia and the Pacific, and there is limited information on their operationalization and status.

To tackle COVID-19, several countries in Asia and the Pacific signed MRAs and MOUs to expand their production and manufacturing capacity of COVID-19 vaccines or to train health-care professionals for vaccine administration. In 2021, for example, India and Japan signed an MOU related to “specified skilled workers” in select sectors, which also covered nursing care. The MOU helped set up an institutional mechanism for partnership and cooperation between the two countries for sending and receiving skilled Indian workers subject to certain requirements (Press Information Bureau 2021). Another example is of an MOU between the Ministry of Health and Family Welfare (India) and the Department of Health and Human Services (US), signed in September 2021, for cooperation on International Centers for Excellence in Research to collaborate in conducting R&D and establishing production facilities related to diagnostics and vaccines. There is also cross-border recognition of vaccines through MRAs. For example, India and Australia in 2021 signed an MRA in which Australia accepted the Bharat Biotech-manufactured Covaxin to facilitate travel between the countries (Mukherjee, Mukherjee, and Goswami 2022). Although MOUs show intent, they may not be binding commitments.
9.3.4 Government Procurement under Trade Agreements

Since the government plays a critical role in the health-care sector, trade agreements can help by including subsidy provisions for pharmaceuticals and medical devices under various government programs, as in the Comprehensive and Progressive Agreement for Trans-Pacific Partnership (Mukherjee, Mukherjee, and Goswami 2022). However, there is limited coverage of health care under government procurement in trade agreements overall. For example, hardly any commitments exist for this sector under the RCEP. Further, the chapter on government procurement in the agreement aims to promote transparent laws, regulations, and procedures and to develop cooperation among the RCEP member states.

The WTO Agreement on Government Procurement mostly covers developed countries. Trade agreements of developed markets such as the US and the European Union also have reasonably good clauses to ensure transparency, clarity, and nondiscriminatory access to government procurement for the health-care sector. However, many developing countries and LDCs in Asia and the Pacific are unwilling to include health care in a government procurement chapter as has been the case of the India–United Arab Emirates CEPA. This is often because the procurement process may vary between central and federal governments and local government agencies, which makes it difficult to ensure transparency and clarity in the entire procurement process.

9.3.5 Intellectual Property Rights

The WTO TRIPS Agreement lays down minimum substantive standards of protection that should be provided for in areas of intellectual property, as well as the procedures and remedies that should be available. The main rule relating to patentability is that patents should be available for any invention, whether a product or process, in all fields of R&D without discrimination.

While most countries in the region are TRIPS compliant, the agreement posed a challenge amid the pandemic when third-party governments needed to produce COVID-19 vaccines without first acquiring the consent of the patent owner (Matthews 2021). Discussions are ongoing in the WTO to temporarily waive certain rules related to TRIPS so as to allow more countries access to vaccines, drugs, and medical technologies as a COVID-19 prevention measure (Labonte and Baker 2021).
9.3.6 Investments in Health Care and Trade Agreements

While investments can be a part of a chapter in trade agreements, they can also be covered under bilateral investment treaties. Investment treaties and membership to platforms such as the International Centre for Settlement of Investment Disputes contribute to increased FDI inflows, as they provide security and commitment to foreign investors and increase their confidence to enter a foreign market (UNCTAD 2020a). To date, countries in Asia and the Pacific have signed about 1,140 bilateral investment treaties. However, social sectors such as health are not often covered in such treaties. If it is, the health sector could be in the exclusion list or have limited coverage. This is an issue as investments in health-care infrastructure have long gestation periods, and firms look at certainty and investment protection before making a cross-border investment. Some recent agreements are bringing more clarity to how investment should be covered in a way to help establish regional supply chains (Box 9.6).

Box 9.6: Republic of Korea’s Free Trade Agreements with Cambodia and Uzbekistan

The 2021 Cambodia–Republic of Korea Free Trade Agreement (FTA) and the 2021 Republic of Korea–Uzbekistan FTA aim to attract more trade and investment. These FTAs allow the Republic of Korea to expand its export market, optimize regional supply chains of key industrial items, and help revive economic activity in a mutually beneficial manner. They are expected to allow Korean investment and transfer of technology and skills to the partner countries, while utilizing their labor, as in Uzbekistan. Health-care companies such as health-care and medical equipment manufacturer ASKO Company Limited have expressed their interest in setting up a factory in Cambodia.

Sources: Cambodia Investment Review (2022); ASEAN Briefing (2022); and Silk Road Briefing (2021).
9.4 Conclusions and Recommendations

Modern trade agreements are complex. They have different provisions such as those related to tariff reduction, ROO, standards, intellectual property protection, trade facilitation, investment, government procurement, and areas of mutual recognition and cooperation, with implications on trade in COVID-19-related health products and vaccines. Most of the existing trade agreements have limited coverage of health products and do not have provisions to address health emergencies like the current pandemic. Trade agreements need to take into account future health emergencies and how countries can work together to address them.

A major issue is vaccine recognition, which is slowing down vaccine administration and delivery across countries. Another issue is vaccine affordability and pricing. While there is a need to ensure affordability and low price, especially in developing countries and LDCs, unless cost is covered and the private sector sees profits, firms will not invest. Trade agreements should also be used to build in resilient vaccine supply chains.

Asia and the Pacific covers a wide range of countries with varying population, growth and development level, health-care needs, and government ability to cover health-care expenditure. It is thus important for an open trading system in the health-care sector to make COVID-19 vaccines easily accessible to all and help tackle the pandemic. Causes of the unequal vaccine distribution include also scattered vaccine and input production sites, financial capacity, and political decisions. Future trade agreements should have comprehensive coverage of the health sector and ensure that countries commit to removing barriers to trade and facilitate smooth cross-border flow of medical goods and health-care practitioners. They need to cover not only tariff reduction but also mutual recognition of standards and ensure that ROO are not an obstruction to establishing supply chains. Vaccines have been developed through cooperation in R&D and clinical trials, but vaccine administration requires multi-stakeholder cooperation both within and across countries and recognition of vaccines by governments. Private sector partnership in vaccine development is important. Aid for trade can cover vaccine for LDCs. Cross-border data flow is needed to monitor the outcome of the vaccines and their impact on patients. It is important to pool resources, share best practices, and exchange information and data. Barriers must be removed to fast-track transport of vaccines through e-commerce and express delivery. The participation of developing countries and LDCs in both plurilateral and bilateral trade agreements should be enhanced to reduce barriers to trade and give businesses a stable operating environment.
Given this background, this section provides some recommendations to enhance trade and investment and facilitate greater collaboration in Asia and the Pacific.

### 9.4.1 Tariffs

Though all countries need vaccines, the sophisticated nature of vaccine production does not allow all countries to produce them as they lack access to special equipment and raw materials and inputs, storage facilities, and highly skilled labor. Thus, trade of vaccines is very important, both as a preventive measure and a mitigation measure against the effects of a pandemic. Ensuring a seamless distribution of vaccines requires zero tariffs or open markets, product recognition, online information hubs, and increased cooperation and coordination. In general, autonomous tariffs for health-care products, especially vaccines and other critical medical goods and devices, should be low. Countries need to study how tariff reductions impact the domestic industry as well as how to prune the negative or exclusion list in trade agreements. Exclusion lists should be kept to the bare minimum. When reducing tariffs, countries need to keep in mind the impact of inverted duties on domestic manufacturing. Lower autonomous tariffs will also help to reduce distortions resulting from multiple trade agreements with different levels of tariff liberalization and different commitments and/or concessions for different trading partners. A trade agreement may include a most-favored-nation clause so that a country can gain from the future trade agreements of their trading partners. Economies like Japan and the European Union include most-favored-nation clauses in their trade agreements.

### 9.4.2 Addressing Non-tariff Measures

Domestic regulations of countries in Asia and the Pacific need to align with international agreements like the WTO SPS and TBT agreements. The standards and requirements (like labeling requirements) have to be clearly defined and published online. The import clearance process for health products should be well-documented, fast-tracked, and made available online.

There needs to be a well-defined domestic system for time-bound approval and testing of drugs, medical devices, and other products. Developing countries may need support in areas such as capacity building for testing authorities and laboratories, and there is scope for cooperation with developed countries and international agencies in this area. Within countries, consultation with multiple agencies from customs to drug controllers and laboratories is encouraged. In this
area, multi-stakeholder consultation and/or collaboration may help. Shortages of human resources and infrastructure have to be identified and addressed.

Trade agreements need to seek time-bound commitments for conformity of standards and processes and for regulatory cooperation. Trade agreements between developed countries and developing countries or LDCs can provide for capacity building and support. They can also establish processes for mutual recognition of standards and testing processes, including mutual recognition of laboratories, third-party certification bodies, and evaluation by drug controllers. It could be of benefit to design a model process that countries can use as a template for the approval of medical goods and drugs. The trade agreements could also lay down a fast-track system for the clearance of drugs, vaccines, and other products related to health emergencies.

9.4.3 Rules of Origin

Rigid ROO restrict global value chain development, and there is a need for ROO harmonization across multiple trade agreements. With multiple FTAs, ROO need to be simple, transparent, and easy to implement.

9.4.4 Intellectual Property Rights

Almost all comprehensive trade agreements in Asia and the Pacific are TRIPS compliant, and some of the agreements with markets like the US and European Union are TRIPS plus. Developing countries need to review the implications of signing TRIPS plus agreements. India had raised the issue of a TRIPS waiver during the pandemic, and discussion needs to take place in international forums and through trade agreements on TRIPS provisions versus health pandemic management.

9.4.5 Trade Facilitation

The WTO Trade Facilitation Agreement should be implemented uniformly across all countries, and trade facilitation should also be covered under trade agreements. One possibility is to have a green channel or fast-track clearances for vaccines. Ports of entry should have appropriate storage and testing facilities for health-care products. These could also be included in trade agreements.

Along with multilateral policy coordination for vaccine supply chains, subsidies and incentives are crucial to expand production and R&D. With respect to COVID-19 vaccines, trade facilitation is essential because of the diverse locations of input producers and vaccine manufacturers.
9.4.6 Sharing Health-Related Data

For clinical trials conducted to understand the side effects of vaccines, there is an urgent need for a policy that protects sensitive patient data while simultaneously allowing for sharing of trusted data to advance R&D, innovation, and current and future pandemic management. Countries need to have domestic regulations on sharing of patient and other health sector data for better service provision, research, and other purposes. A type of data sharing agreement like the European Union’s General Data Protection Regulation can be a starting point.

9.4.7 General Foreign Investment-Related Requirements

Countries and governments need to engage in discussion with stakeholders to understand the reasons for restrictions on FDI. Where such limits exist, they may be relaxed for health infrastructure such as hospitals, diagnosis centers and clinics, and similar facilities to help build up infrastructure in developing countries and LDCs.

As countries sign trade agreements, they should ensure that the health sector is covered in these agreements and their investment chapters. To identify concerns related to bilateral investment treaties, a model treaty may be created based on consultations. Furthermore, countries need to discuss the implication of the health-care sector in emergency situations such as a pandemic in international forums like the International Centre for Settlement of Investment Disputes.

9.4.8 Temporary Movement of Health-Care Professionals

Greater international collaboration is needed in health services to help mobilize a pool of health professionals to fight emerging health issues and reduce human resource shortages. Easy mobility of health-care professionals is also crucial for the administration of COVID-19 vaccines, which require mutual recognition of degrees of nurses and other health-care workers.

9.4.9 Government Procurement

Many developing countries and LDCs in Asia and the Pacific need a robust domestic public procurement policy that covers national, provincial, and local governments.
It also important that the health sector be covered under a government procurement chapter in trade agreements. There should be no bias or pre-approved vendors, the bidding process should be competitive, and procurement at both the central and provincial government levels may be covered under trade agreements.

9.4.10 Mutual Recognition Agreements, Memorandums of Understanding, and Other Collaboration

Maintaining uniformity of standards and processes within countries will help when negotiating MRAs and/or MOUs related to the faster approval and recognition of vaccines in partner countries. They can also cover the recognition of health products and degrees conferred by the partner countries’ institutions. In addition, countries need to increase public–private partnerships and partnerships between various health-care stakeholders to promote collaboration among countries. A partnership framework to enable developing countries and LDCs to improve private sector participation is also helpful. More active participation in trade agreements and shortened lead time for implementation works greatly to the advantage of all countries. For instance, despite the rigidities in its health sector policies, Viet Nam has been forthcoming in participating in trade agreements and has gained from such participation. ASEAN as a region has progressed well in terms of enhancing trade, investment, and collaboration among its members. There are several examples of best practices in the region that can be replicated across countries in Asia and the Pacific.

Furthermore, there is need for collaboration in disaster management and national emergency preparedness in terms of health care, focusing on more resilient supply chains, better manufacturing and production capabilities, and easier frameworks for data sharing and R&D, so that countries are better prepared to mitigate the impact of emergencies.
References


From Lab to Jab: Improving Asia and the Pacific’s Readiness to Produce and Deliver Vaccines


10

Innovative Approaches to COVID-19 Vaccine Approvals: Lessons in Regulatory Cooperation and Collaboration

Simon Lacey and Andrew D. Mitchell

10.1 Introduction

This chapter explores how national regulatory authorities (NRAs) cooperated in developing, testing, approving, manufacturing, and distributing coronavirus disease (COVID-19) vaccines at a speed never before witnessed in human history. With a focus on Asia and the Pacific, this chapter highlights what regulators worldwide did right and where the COVID-19 pandemic revealed gaps in policies and working procedures. This chapter also discusses what lessons can be learned to increase readiness among NRAs to better prepare them for future health crises.

Section 10.2 begins by summarizing how medicines (of which vaccines are a subset) are regulated today, including the goals governments generally pursue in this policy area. Section 10.3 examines in more detail how international regulatory cooperation functions in the area of medicines. Section 10.4 then discusses the extraordinary levels of international cooperation witnessed in response to COVID-19, which saw governments, the private sector, and nongovernment organizations

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working together in unprecedented ways. Following this, section 10.5 examines regulatory cooperation in vaccines in Asia and the Pacific.

Of course, international regulatory cooperation in vaccines is a small subset of international regulatory cooperation in medicines. Although it has taken center stage recently due to COVID-19, it is embedded in the broader inter-NRA cooperation processes. Hence, our discussion is also framed within the broader structures that characterize international regulatory cooperation in medicines.

Penultimately, section 10.6 considers the present outlook and makes recommendations to entrench the momentum achieved during the pandemic on regulatory harmonization, so the many lessons learned are not lost and the state of preparedness for future public health crises does not regress to pre-COVID-19 levels. Finally, section 10.7 concludes the analysis.

10.2 Regulation of Medicines

This section contextualizes the regulation of vaccines within the broader framework of regulating medicines. It begins by discussing different aspects of how medicines are regulated today and then highlights how different regulatory approaches tend to vary between countries and regions. It then discusses how different public health crises (and the political backlashes they inevitably give rise to) have historically proven to be important catalysts for new medical breakthroughs and regulation of the sector. Next, this section discusses some processes and procedures at the heart of modern regulation of this sector. Finally, it discusses the technical complexity and governance challenges that pervade modern regulatory systems.

10.2.1 Different Aspects of Modern-Day Regulation

The distribution and consumption of medicines are regulated to varying extents in almost all countries today. Regulation typically covers several areas, including but not limited to (i) evaluation of data on the safety and efficacy of new drugs throughout various trial stages; (ii) inspection and certification (licensing) of manufacturing facilities and distribution channels against contamination risks; (iii) pre- or post-marketing monitoring of any reported adverse drug reactions; and (iv) assurance that safety and efficacy claims made about approved medicines in promotional and advertising materials are accurate (drug regulation and approval).²

² Wang and Wertheimer (2021) incorporate other activities into this list, including development of regulatory policy and guidance, surveillance priorities and inspection programs, enforcement action clearance responsibility, and testing research.
International regulatory cooperation occurs to varying degrees across areas (i) to (iv) but is arguably the most widespread in areas (i) and (ii). Accordingly, most of this chapter’s analysis relates to these two functions and focuses on how they can be strengthened and improved via international cooperation.

10.2.2 Regulatory Variance

Comparative studies have shown that despite efforts over the past 30 years at regulatory harmonization—starting in Europe but also in other regions such as Southeast Asia, East Africa, and the Americas (Ndomondo-Sigonda et al. 2021; PAHO 2019; Regi 2017)—a high degree of variance remains between countries as to the form that regulatory procedures take, their duration, complexity, cost, and the compliance burden they impose more generally (Dukes 1986; Pezzola and Sweet 2016). This has downstream impacts on industry structures (Daemmrich 2009) and people’s access to medicines (Roth et al. 2018). These variations persist despite most agencies sharing the same goal: ensuring that new drugs are safe, efficacious, and of high quality (NASEM 2020).

10.2.3 Progress through Crisis Response

Establishing and improving the regulation of medicines, particularly in advanced industrialized countries, has often advanced in response to a specific health crisis. For example, Ballentine (1981) and Thind and Kowey (2015) discuss the 1937 Elixir Sulfanilamide Incident in the United States (US), in which 105 people were fatally poisoned, resulting in a public outcry and demands for congressional action that culminated the following year in the Federal Food, Drug, and Cosmetic Act.3 Abed (2014) discusses the role the thalidomide tragedy of the 1960s played in forming new regulatory agencies throughout Europe. Daemmrich (2009) details the impact the AIDS crisis had on the US Food and Drug Administration (FDA), particularly concerning expedited approval of new and experimental medicines and treatments, and notes that the corresponding dynamic was largely absent from the European regulatory scene. As we will show later, the current COVID-19 pandemic has had a similarly dramatic impact on several aspects of the regulatory approval process at the national level and on international regulatory cooperation in vaccines.

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3 21 U.S.C. ch 9 § 301 et seq.
10.2.4 Processes and Procedures

The procedures for gaining approval differ between countries, although some commonalities exist. One of the most important and resource-intensive steps, and indeed, the first step characterized by the involvement of the regulator, is submitting an application by the sponsoring drug maker to investigate a new potential drug. In the US, this is an Investigational New Drug (IND) application (FDA 2021; Holbein 2009). In the European Union (EU), the member states’ NRAs approve and oversee clinical trials conducted on their respective populations, subject to standards and procedures adopted under EU law (EMA 2019).

The IND application with the FDA seeks approval to proceed with human clinical trials. It generally includes information the drug maker has compiled (in preclinical testing) on three essential test criteria: (i) toxicity and pharmacology of the drug demonstrate that the drugs can be safely administered to human test subjects; (ii) the ability to safely and consistently manufacture large batches of the drug to the same levels of quality; and (iii) the proposed clinical protocols, including a demonstration of the competency of those conducting the trials and the informed consent documents of those on whom said trials will be performed (Thind and Kowey 2021). These three criteria represent a high barrier for drug makers to clear. Lesko and Woodcock (2004) posit that over 80% of new drug candidates that begin the IND application process fall by the wayside by failing to meet one or more of these criteria.

Human clinical trials occur in three phases. Phase I involves small numbers (between 20 and 80) of healthy volunteers. The main objective of this phase is to identify both side effects and how the body metabolizes and excretes the drug (FDA 2017). Phase II trials involve several hundred test subjects, all afflicted with the condition that the drug is intended to treat. Here, the emphasis is on determining the drug’s efficacy, particularly determining a so-called therapeutic dosage window. This is a dose at which “the efficacy and side effects are optimally balanced” (Thind and Kowey 2020, p. 3961). Finally, Phase III trials involve a significantly larger number of test subjects (from several hundred to several thousand) and involve “studying different populations and different dosages and using the drug in combination with other drugs” (FDA 2017).

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4 Here, our discussions are grounded primarily on the processes and procedures (and terminology) established and followed by the US FDA.
Only after Phase III trials have been successfully concluded does the sponsoring drug maker submit a New Drug Application (NDA), again to the FDA. If the application document is complete (a factual determination the FDA has 60 days to make), the FDA begins its review, which includes the research findings resulting from the entirety of preclinical and clinical trials, information that will be provided to consumers on the drug’s labeling, and the facilities where the drug is manufactured (FDA 2015).

10.2.5 Technical Complexity and Governance Challenges

The inherent technical complexity of approval procedures comes in various forms—both in terms of the scientific and clinical knowledge required and the governance structures that should ideally be in place to properly manage conflicts of interest and external pressures. Addressing these is essential if the regulator is to perform its objective: ensuring that drugs are safe, efficacious, and of high quality. Even in advanced industrialized countries, this can be a source of significant challenges for regulators. There is a critical development dimension here, given that many developing countries will lack either or both preconditions (Pezzola and Sweet 2016).

10.3 International Regulatory Cooperation in Medicines

This section discusses the evolution of regulatory cooperation between different NRAs and how this process functioned before COVID-19 (discussed in section 9.4). It begins with the European experience, since this is where international regulatory cooperation between different NRAs was successfully pioneered. It then turns to the factors

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5 WHO distinguishes between four categories or “maturity levels” in terms of the technical and regulatory capacities of NRAs and the governance systems within which they operate. Level 1 is the least mature, and Levels 3 and 4 are the most mature. Using its Global Benchmarking Tool (GBT), WHO has determined that with respect to the current status of regulatory systems for medicines and vaccines, about 100 countries are at Maturity Level 1, meaning only some elements of a regulatory system exist. Another 44 countries are at Maturity Level 2, meaning that an evolving regulatory system is present that partially performs essential regulatory functions. Further, the 144 countries that together constitute Maturity Levels 1 and 2 can only ensure the quality of medicines on their markets if they rely on the regulatory systems of the 50 countries that have medical regulatory systems at Maturity Levels 3 and 4 (WHO 2021c).
driving regulatory cooperation and the forms it takes today. After that, this section discusses several multilateral and regional approaches to regulatory cooperation (section 9.5 offers an in-depth appraisal of this in Asia and the Pacific).

10.3.1 History: The European Experience

The forerunner of what we today understand as international regulatory cooperation in medicines emerged over several decades in the context of European economic integration efforts. In 1965, Council Directive 65/65/EEC\(^6\) sought to approximate procedures and standards in several important ways, including:

- the principle that no medicine shall be placed on the market without approval (Art. 3);
- a set of minimum requirements for drug makers to meet before approval can be granted (Art. 4);
- time limits, within which national regulators must review and decide upon applications for market approval from drug makers (Art. 7);
- the period for which such approvals are to be valid (Art. 10);
- enforcement actions related to post-market surveillance (Art. 11); and
- minimum requirements for drug labeling (Arts. 13–19).

In 1975, two new directives were adopted: one on clinical testing of medicines before their marketing approval (Council Directive 75/318/EEC)\(^7\) and another on facilitating the placing of medicines already authorized in one member state on the market of another, based on mutual recognition (Council Directive 75/319/EEC)\(^8\). The directives also established the first supranational body in the regulation of medicines in the EU: the Committee for Proprietary Medicinal Products (CPMP), intended to “help EU Member States to adopt a common position with

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regard to decisions on issuing a marketing authorisation” (Abed 2014, p. 117).

The CPMP’s activities enabled national regulators and experts to collaborate and build the trust essential to deeper and more formalized expressions of regulatory cooperation (Golberg 2020). More importantly, the development, by experts from governments, industry, and academia, of detailed technical guidelines covering many aspects of the approval process—including quality, safety, efficacy testing, and good manufacturing practices—grounded broader international cooperation and harmonization.

Today’s successor to the CPMP is the Committee for Medicinal Products for Human Use of the European Medicines Agency (EMA). The CPMP conducts the scientific evaluation of marketing authorization applications and opines on whether to approve a drug for marketing to the general public. This is then forwarded to the European Commission, which subsequently issues a legally binding decision.

10.3.2 History: International Regulatory Cooperation

In 1990, the EU, US, and Japan launched the International Conference for the Harmonisation of Pharmaceutical Requirements, aiming to “reduce unnecessary repetition of tests in humans and animals and duplication of costly stability and quality controls (...) without compromising public health” (Sauer 2019). It brought together government regulators and associations representing the research-based pharmaceutical industries in these regions (Lindström-Gomers and Mullin 2019). Over time, participation in biannual meetings grew to include experts and regulators from WHO, Canada, Switzerland, and the global industry body, the International Federation of Pharmaceutical Manufacturers and Associations. Regional events superseded this mostly informal system of regular meetings and ongoing working groups and in 2015 the establishment of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), with 16 members and 33 observers from all regions of the world.

Collaboration under the auspices of first the Conference and later the Council has produced an array of guidelines under four distinctly classified areas: quality, safety, efficacy, and multidisciplinary (i.e., crosscutting). As the ICH (2021) notes, some of the harmonization outcomes achieved in the quality category include “defining relevant thresholds for impurities testing and a more flexible approach to pharmaceutical quality based on Good Manufacturing Practice (GMP) risk management.” The ICH touts some of its achievements in safety, including “a comprehensive set of safety Guidelines to uncover potential
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risks like carcinogenicity, genotoxicity and reprotoxicity” (ICH 2021). After decades of cooperation, several important outcomes have been achieved, including the Electronic Common Technical Document, a set of widely accepted norms such as a common electronic format for applications, and the Medical Dictionary for Regulatory Activities, a common terminology (Lindström-Gommers and Mullin 2019; Sauer 2019).

10.3.3 Factors Driving Regulatory Cooperation

One factor driving regulatory cooperation is the asymmetry in resources and capabilities between NRAs. Drug regulation is complex and highly resource-intensive. Only a handful of NRAs worldwide can effectively manage the entire ambit of regulatory activities, spanning pre-marketing approval to post-marketing surveillance (Olsson et al. 2010; Pezzola and Sweet 2016). Even the most well-resourced and technically sophisticated NRAs struggle to fulfill their mandates to the complete satisfaction of all relevant stakeholders (e.g., drug companies, the public, doctors, patient advocacy groups, public health nongovernment organizations [NGOs], political leaders, and others). Thus, it is unavoidable that NRAs must “consider enhanced, innovative, more effective forms of collaboration to make the best use of the available resources and expertise, avoid duplication and concentrate their regulatory efforts and resources where they are most needed” (WHO 2021b, p. 240).

Another factor is the growing complexity of supply chains. NASEM (2020, preface) noted that “[drug] development, authorization, and regulatory supervision have become international endeavors, with most medicines now being global commodities.” Indeed, “China is now the leading producer and exporter of APIs [active pharmaceutical ingredients] by volume, manufacturing more than 2,000 APIs” (NASEM 2020, p. 72). India has also become a major production center. Its pharmaceutical sector “accounts for 71% of the market share of generic drugs and supplies more than 50% of the world’s vaccines” (NASEM 2020, p. 73). The authoring committee concludes that “protecting and promoting public health in a time of globalization,” “unprecedented advances in technology,” and “growing complexity of medicines and the supply chains for their manufacture and production – is the single greatest challenge facing medicines regulatory authorities today” (NASEM 2020, p. 28).
10.3.4 Forms of Regulatory Cooperation

Regulatory cooperation between different NRAs takes various forms, both formal and informal. In a technical briefing prepared in the context of capacity-building efforts under its Global Benchmark Tool, WHO defines one of the objectives of its Regulatory System Strengthening program as promoting regulatory cooperation, convergence, and transparency through three activities: (i) networking, (ii) work-sharing, and (iii) reliance (Khadem 2019).

A. Networking

Inter-NRA networking has occurred for several decades thanks to the regular meetings organized under the auspices of the International Conference for the Harmonisation of Pharmaceutical Requirements. Although this first began between US, EU, and Japanese regulators, it soon expanded to include experts from other well-resourced regulatory bodies in countries such as Canada, Switzerland, Australia, and New Zealand. It was finally opened up more broadly and became formalized as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (discussed earlier).

Various other forums allow regulators from different NRAs to meet informally, and to discuss and share knowledge and experience on different areas of substantive expertise. The most important is WHO, which organizes dozens of meetings annually in Geneva and at the regional level. Other multilateral and regional organizations do the same, such as the WTO, the United Nations, the World Bank, the Asian Development Bank, Asia-Pacific Economic Cooperation (APEC), and the Association of Southeast Asian Nations (ASEAN) (regional cooperation efforts are discussed in more detail in section 10.3.7).

Networking activities between regulatory agencies may include twinning, staff visits, and exchanges (Ndomondo-Sigonda et al. 2017; WHO 2021b). For example, from December 2010 to June 2011, the Croatian NRA HALMED\(^\text{10}\) was twinned with its Spanish counterpart AEMPS.\(^\text{11}\) This program involved 11 visits by 30 AEMPS officials to

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\(^9\) The other objective of this program – in fact the first, as the name Regulatory System Strengthening suggests – is to “build regulatory capacity in Member States consistent with good regulatory practices.”

\(^\text{10}\) HALMED stands for Agency for Medicinal Products and Medical Devices of Croatia.

\(^\text{11}\) AEMPS stands for Spanish Agency for Medicine and Health Products.
conduct training seminars and workshops and two study tours by HALMED staff to the Spanish official medical control laboratory network partner (Tomić 2011).

B. Work-Sharing
A recent WHO technical report describes work-sharing as “[a] process by which NRAs of two or more jurisdictions share activities to accomplish a specific regulatory task.” It goes on to note that “[t]he opportunities for work-sharing include joint assessment of applications for authorisation of clinical trials or marketing authorisations, joint inspections for good practices, joint post marketing surveillance of the quality and safety of medical products, joint development of technical guidelines or regulatory standards and collaboration on information platforms and technology” (WHO 2021b, p. 244). Work-sharing is thus an important mechanism for building trust between NRAs, which is an essential prerequisite for them to be able to meaningfully practice reliance (discussed immediately below) (NASEM 2020). For example, the Australia–Canada–Singapore–Switzerland–United Kingdom ACCESS Consortium aims “to maximise international cooperation, reduce duplication, and increase each agency’s capacity to ensure consumers have timely access to high quality, safe and effective therapeutic products” (TGA 2023).

A distinct form of work-sharing is a joint activity, assessment, or inspection. Here, the goal is not to avoid duplication so much as to encourage it under the mantra of two sets of eyes see better than one. WHO describes this sort of arrangement as “a form of work-sharing whereby a regulatory task is conducted by two or more NRAs in collaboration to share their assessments, benefit from each other’s expertise and discuss any shortcomings of the data evaluated” (WHO 2021b, p. 244). In the case of a joint assessment, an application may be submitted to two separate NRAs, allowing them to conduct their evaluations concomitantly and share findings and conclusions. This reduces the possibility that an important factor may be overlooked or underappreciated. Similarly, a joint inspection involves staff from two NRAs inspecting the same facilities (either simultaneously or asynchronously), with each NRA being tasked with different aspects of the inspection (WHO 2021b).

C. Reliance
The most important instance of regulatory cooperation is reliance, which manifests in various ways along a gradient of increasing formality. The abovementioned NASEM report refers to a range of approaches and methods to facilitate reliance (and recognition, discussed later). It acknowledges that these can be more or less formalized in their conceptualization and operation. For example, establishing ad hoc
committees, working parties, or other dedicated working groups assembled to focus on a specific active pharmaceutical ingredient or set of processes is less formal. On the other hand, memorandums of understanding (MOUs), confidentiality agreements, or mutual recognition agreements (MRAs) are more formal instruments.

Reliance can also be categorized as either horizontal or unidirectional. The former occurs between NRAs that operate at roughly the same level of technical sophistication and resource endowment, such as those discussed earlier in the context of the ACCESS Consortium or between the EMA and the FDA. On the other hand, unidirectional reliance involves less well-resourced NRAs, particularly those in developing countries, relying on the regulatory decisions or work products (assessment reports, etc.) of better-resourced NRAs, particularly those in advanced industrialized countries.

D. Recognition
NASEM (2020) describes recognition as “the ultimate form of reliance.” WHO calls it “a special and more formalised approach to reliance,” where one NRA recognizes “the decisions of another regulatory authority, system or institution, obviating additional regulatory assessment to reach its own decision” (WHO 2021b, p. 245). Some NRAs, however, are unwilling to share completely unredacted decisions or assessment reports, representing a serious constraint on the ability of dependent NRAs to rely on these works (NASEM 2020). Accordingly, NASEM (2020, p. 13) advocates sharing of unredacted documents.

E. Mutual Recognition
Mutual recognition is very important in inter-NRA regulatory cooperation. It is a formal instrument whereby two NRAs agree to recognize each other’s decisions and/or work products. It is usually predicated on binding agreements between the cooperating NRAs or governments (as treaties) (WHO 2021b). The 2020 NASEM report lists 14 MRAs currently in force in regulating medicines, all of which are between “most mature” NRAs under the WHO nomenclature (Khadem Broojerdi et al. 2021). These MRAs typically concern issues or processes such as GMP inspections, batch certifications, product packaging, labeling standards, conformity assessment requirements, GLP inspections, and acceptance of industrial products (NASEM 2020).

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12 These terms are borrowed from the 2020 report of the US National Academies of Sciences, Engineering and Medicines cited.

13 The 14 MRAs in question are all between NRAs in either Australia, Canada, the EU, Israel, Japan, Iceland, Lichtenstein, New Zealand, Norway, and the US.
Several proposals to increase the impact of mutual recognition include decoupling them from trade agreements (where they are usually negotiated) so that they may be bilaterally concluded between NRAs directly. Arguably, this would allow these arrangements to be completed more quickly and without them necessarily being held hostage to the other (unrelated) bargaining and horse-trading that inevitably make the negotiation of trade agreements such a protracted and often tortuous process. Another recommendation is to expand their substantive scope beyond the issues they currently cover (see immediately above).

10.3.5 Multilateral-Driven Cooperation by the World Health Organization

WHO is a significant actor in its contribution to inter-NRA cooperation. This chapter has already discussed WHO’s efforts in regulatory systems strengthening through its Benchmarking Tool (WHO 2021d). Other ways in which WHO supports regulatory strengthening and harmonization activities include developing common standards for pharmaceutical processes and regulation and supporting the regional cooperation mechanisms discussed. WHO’s Prequalification Programme can result in accelerated marketing authorizations for medicines in as little as 3 months (ADB 2016).

10.3.6 International Coalition of Medicines Regulatory Authorities

The International Coalition of Medicines Regulatory Authorities (ICMRA) was established in 2012 in the face of growing recognition by the heads of several NRAs of the need for coordinated leadership to “address current and emerging human medicine regulatory and safety challenges globally, strategically and in an ongoing, transparent, authoritative and institutional manner” (ICMRA 2021). The issues addressed by this initiative include the growing complexity in both “manufacturing and distribution supply chains for medicinal products” and “medicinal products and their ingredients (e.g. new chemical entities and innovative drugs)” (ICMRA 2021). The ICRMA comprises 24 member NRAs from countries such as Australia, the EU, the US, Japan, the Republic of Korea, Mexico, India, Nigeria, South Africa, and the People’s Republic of China (PRC) (ICMRA 2021). It also has associate members from 13 countries at different maturity levels and counts WHO as a permanent observer. As discussed in section 10.4, the ICMRA assumed a key function in the race to approve and distribute vaccines at the height of the COVID-19 pandemic.
10.3.7 Regional Cooperation Mechanisms

Several regional initiatives have proven highly effective at promoting cooperation across regions as diverse as East Africa, Southern Africa, the Americas, Asia, and the Pacific. For example, the so-called ZAZIBONA process (involving NRAs from Zambia, Zimbabwe, Botswana, and Namibia) is a collaborative procedure for the registration of medicines under the auspices of the Southern African Development Community. It succeeded in shortening timelines for drug approvals in the participating countries from years to months (Ndomondo-Sigonda et al. 2021).

In the Americas, the Pan American Network for Drug Regulatory Harmonization has, among other achievements, successfully initiated “harmonization activities for small molecule i.e. nonbiological, less complex medicines” (ADB 2016) and drafted Guidelines on Good Regulatory Cooperation Practice. These guidelines went on to be universally adopted by WHO.

In Asia, the ASEAN Pharmaceutical Products Working Group “has developed its own guidelines on technical requirements and what information marketing authorization applications should include” (ADB 2016). The Asia-Pacific Economic Cooperation (APEC) Life Sciences Innovation Forum, meanwhile, regularly convenes a Regulatory Harmonization Steering Committee, which aims to “promote a coordinated approach to medical product regulatory harmonization and capacity-building efforts within the APEC region” (ADB 2016). This chapter discusses regulatory cooperation in Asia in more detail in section 10.5.

10.4 Intergovernmental Cooperation and COVID-19

10.4.1 Initial Responses from the Group of Twenty

In the initial weeks and months of the COVID-19 pandemic, countries scrambled to acquire scarce resources (Bradley 2020; OECD 2020; Tooze 2021). This period was primarily one of competition and not cooperation, but this quickly changed. By the end of March 2020, barely 2 weeks after WHO had declared the outbreak a pandemic, the Group of Twenty (G20) leaders convened an extraordinary summit and pledged a series of actions, including (G20 2020):

• sharing timely and transparent information;
• exchanging epidemiological and clinical data;
• sharing materials necessary for research and development;
expanding manufacturing capacity to meet the increasing needs for medical supplies; and
• ensuring these are made widely available, at an affordable price, on an equitable basis.

Further, the G20 leaders committed to “clos[ing] the financing gap in the WHO Strategic Preparedness and Response Plan” and “provid[ing] immediate resources to the WHO’s COVID-19 Solidarity Response Fund, the Coalition for Epidemic Preparedness and Innovation (CEPI) and Gavi, the Vaccine Alliance” (G20 2020a). One tally counted about $21 billion in pledged financing to support “diagnostics, vaccines, therapeutics, and research and development” (Reuters 2020). This statement was followed by others from G20 leaders over the year, culminating in the Declaration of G20 Health Ministers, adopted in Rome in early September (G20 2020b).

10.4.2 Multilateral Responses from Diverse Sectors

In April 2020, shortly after the G20 meeting, a broad coalition of different partners assembled under the joint leadership of the European Commission, France, and WHO to establish the Access to COVID-19 Tools Accelerator (ACT). The ACT pooled the resources, capabilities, and energies of “governments, global health organisations, manufacturers, scientists, private sector, civil society and philanthropy” (Berkley 2020). One of the most important outcomes of this effort was COVAX, a multilateral response involving governments, the private sector (vaccine manufacturers), and NGOs such as Gavi and CEPI. By early 2022, COVAX had shipped more than 1 billion vaccine doses to 144 countries, with 191 countries participating in the initiative (the vaccine distribution effort is discussed in more detail later). Another important feature of COVAX, which distinguishes it from purely national approaches, is the diversity of its vaccine portfolio. As Gavi has articulated, “COVAX has the world’s largest and most diverse portfolio of COVID-19 vaccines, and as such represents the world’s best hope of bringing the acute phase of this pandemic to a swift end” (Berkley 2020).

10.4.3 The Race to Develop and Mass-Produce a Vaccine

Several COVID-19 vaccines were successfully developed, approved, and then mass-produced at an unprecedented speed (Tooze 2021). As Norberg (2020) notes, just 6 weeks after PRC researchers published the viral genome, a US biotechnology company was able to notify authorities
of a new vaccine candidate to conduct clinical trials. As early as 2 April—and thus less than a month after WHO had declared a pandemic—“America’s National Library of Medicine listed 282 potential drugs and vaccines against the new virus and were [sic] already recruiting patients or proposing to do just that” (Norberg 2020).

Ordinarily, vaccine development takes about 10–15 years (The College of Physicians of Philadelphia 2018). Before COVID-19, the fastest-developed vaccine had been for mumps, which took 4 years (Cohen 2020; Solis-Moreira 2021). Given COVID-19’s catastrophic impact—on countries’ public health systems, economies, and the social fabric of cities and communities globally—it was imperative that a vaccine be found as soon as humanly possible. WHO coordinated an international response that pooled information, allowed researchers to agree on the most promising candidates, and subsequently scaled up clinical trials across multiple countries (DGC 2020; Voysey, Costa-Clemens, and Mahdi 2020).

With applications being reviewed for different vaccine candidates by stringent regulatory authorities, such as the UK’s Medicines & Healthcare Products Regulatory Agency (MHRA) and the US FDA, the first emergency use authorizations started to be issued in December 2020.14 WHO gave an Emergency Use Listing (EUL) for the Pfizer–BioNTech vaccine on 31 December 2020, thereby “[opening] the door for countries to expedite their own regulatory approval processes to import and administer the vaccine” (WHO 2020).

10.4.4 Making a Virtue of Necessity through Regulatory Agility

Against this backdrop, NRAs made a virtue of necessity by developing or expanding upon regulatory agility (Bolislis, Lucia de Lucia, and Dolz 2021; Lim 2021) to a degree hitherto unimaginable.

For example, Avorn and Kesselheim (2020) note that in June 2020, the FDA stated its willingness to entertain “less conventional approaches,” one of which would be to allow for “accelerated approval” of a vaccine candidate, based not on the results of Phase III clinical trials but rather based on “antibody levels or another biochemical marker” (Avorn and Kesselheim 2020, p. 1284). On 11 December 2020, the FDA authorized the Pfizer–BioNTech COVID-19 vaccine under an

Emergency Use Authorization (EUA), relying on results from Phase III trials involving 37,586 participants who were enrolled “in an ongoing randomized, placebo-controlled international study,” with the majority of participants being in the US (FDA 2020).

A second example of regulatory agility was the formation within COVAX (discussed earlier) of a Regulatory Advisory Group, co-led by WHO and CEPI, comprising representatives from 10 NRAs from different countries and regions. This group was to deliberate upon and provide feedback concerning vaccine development by different manufacturers. For example, for vaccine developers to obtain more coordinated feedback from NRAs, the Regulatory Advisory Group recommended that developers “simultaneously approach several agencies in parallel, e.g. four, including at least one stringent regulatory authority, in different geographic regions with the same data package and give permission to allow the agencies to exchange information and discuss a coordinated feedback” (WHO 2021b, p. 2).

A third example of innovative approaches, under the mantra of regulatory agility, alleviated the burden on vaccine developers in GMP inspections. Here, regulators, in light of travel restrictions and other difficulties, initially offered that GMP inspections “could be facilitated by mutual recognition of GMP inspections done by a stringent regulatory authority” (WHO 2021a, p. 4) before several NRAs such as the EMA, the US FDA, Health Canada, the Health Sciences Authority of Singapore and the Therapeutic Goods Administration of Australia developed additional processes including remote and/or virtual inspections (WHO 2021a).

A fourth agile and collaborative example was COVAX’s establishment of the Support Work to Advance Teams (SWAT). The SWAT comprised groups of experts dedicated to “resolving technical issues and challenges common across all COVID-19 vaccine development projects” (McGoldrik, Gastineau, and Wilkinson 2022, p. 1217). For instance, a Manufacturing SWAT was established, with representatives from regional and global industry associations, to focus on several manufacturing challenges, such as securing sufficient capacity for the initial production and then scaling of vaccine supplies, securing raw materials and other supply chain concerns, and supporting batch release testing (McGoldrik, Gastineau, and Wilkinson 2022, p. 1217).

These and numerous other examples show that as the pandemic spread and its health and economic effects became increasingly

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15 The countries and regions from which representatives of 10 NRAs constituted the Regulator Advisory Groups were Argentina, Australia, Brazil, Canada, Europe (EMA and the European Directorate for the Quality of Medicines & HealthCare), Ghana, Japan, Singapore, and the US.
intolerable politically, regulators scrambled to pull out all the stops to rapidly test and approve new vaccines. Yet, they did so while adhering to the highest scientific rigor and medical safety standards. These standards had long been forming as part of regulatory collaboration initially between a small group of stringent regulatory authorities—but which, over time, became more inclusive. These efforts were afforded legitimacy thanks to their close association with organizations like WHO and multi-stakeholder initiatives like COVAX and CEPI.

10.5 Regulatory Cooperation and Vaccines in Asia

Compared to other regions, many Asian countries managed to perform relatively well in developing new vaccines and successfully executing national vaccine rollouts. The region played host to some of the countries that most quickly vaccinated a significant portion of their populations, such as Singapore, and—after initial stumbles—Australia. Even LDCs such as Cambodia achieved high vaccination rates relatively quickly. But governments varied in their responses to COVID-19 across the region. Indeed, under-resourced public health systems and a lack of administrative capacity to navigate recurring outbreaks as new variants emerged challenged several governments.

10.5.1 Asian Development Bank-Led Initiatives

As a regional development bank with deep ties to and intricate knowledge of Asia and the Pacific, and as an established presence thanks to in-country offices, almost no organization was better placed than the Asian Development Bank (ADB) to identify and address the most urgent socioeconomic challenges confronting economies as the pandemic unfolded across the region—and this was true concerning both the public health and economic impacts of the virus.

A. Asia Pacific Vaccine Access Facility

In December 2020, ADB proposed the Asia Pacific Vaccine Access Facility (APVAX) in response to the resource constraints faced by many developing country members of the regional development bank (ADB 2020). The initiative was a $9 billion financing facility comprising two core components. The first was a rapid response element intended to provide quick access to diagnostic resources and vaccines. The second was financing and support toward long-term and systemic efforts to improve distribution, including transport, storage, and administration. This component also supported institutional capacity building and
post-market surveillance (ADB 2021b). As of September 2021, ADB reported that it had “committed a total of $20.8 billion to the COVID-19 response including vaccination support in its developing member countries. Of this, assistance to the private sector totals $4.9 billion. Under APVAX, ADB has committed a total of $2.3 billion” (ADB 2021b).

B. Budgetary Support for Thailand
In addition to APVAX, ADB supported individual developing country members under various country-specific programs. For example, through the COVID-19 Active Response and Expenditure Support Program, the multilateral development bank loaned $1.5 billion to the Government of Thailand to support its response to the pandemic. Thai authorities used these funds to support a domestic stimulus program and make cash payments to those most economically impacted by COVID-19, particularly in sectors such as tourism and related services (ADB 2020).

10.5.2 Association of Southeast Asian Nations Initiatives

Efforts by ASEAN at closer regulatory cooperation in medicines (and thus vaccines) long preceded COVID-19. Starting with the 1994 Bogor Declaration, ASEAN had been trying for years to integrate the different national economies more closely to form a single regional market (Lätzel 2007). Here, we detail these initiatives concerning regulatory cooperation in medicines and show how, like in other regions, COVID-19 resulted in a slew of new approaches and heightened cooperation.

A. Pharmaceutical Product Working Group
The Pharmaceutical Product Working Group (PPWG) resulted from broader efforts to eliminate technical barriers to trade under processes that were part of ASEAN’s 1992 Free Trade Area, particularly those of its Consultive Committee on Standards and Quality (Lätzel 2007). The PPWG was established in 1999 to support two objectives. The first was removing technical barriers to trade in pharmaceutical products. The second was facilitating access to these products in ASEAN “without compromising” their “safety, efficacy and quality.”

Over the years, the PPWG has achieved notable successes in areas such as harmonized requirements for the ASEAN Common Technical

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Dossier and the ASEAN Common Technical Requirements (both achieved in 2008), or a regional MRA on GMP (also in 2008) and for Bioequivalence Study Reports of Generic Medicinal Products (2018). However, the reality immediately before the COVID-19 pandemic was that regulatory processes for obtaining marketing authorizations were still “highly country-specific” and this “despite regional harmonization efforts” (Tongia 2018).

B. Joint Assessment Coordination Group

The Joint Assessment Coordination Group (JACG) was launched under the auspices of WHO in 2017 as a mechanism for streamlining pharmaceutical approvals across participating ASEAN member states. Under the scheme, a single marketing authorization application is simultaneously filed with all participating ASEAN NRAs, who then collaborate to produce a joint assessment report (HSA 2016). This procedure aims to facilitate authorization procedures, and thus expedite access to medicines that are tested and therefore are deemed to be safe, of high quality, and efficacious. It is also a capacity-building exercise under WHO’s existing regulatory systems strengthening efforts (discussed earlier). To qualify for the procedure, drug candidates already had to have gained (at least tentative) approval by at least one stringent regulatory authority (generally the EMA or the US FDA) or have been prequalified by WHO. Another qualifying criterion for admission to the procedure is that the drug candidate must be aimed at treating a priority disease in the ASEAN region (HSA 2020).

C. ASEAN-OECD Good Regulatory Practices Network

The ASEAN-OECD Good Regulatory Practices Network (GRPN) is a joint initiative led by the Organisation for Economic Co-operation and Development (OECD) and co-chaired by New Zealand and Malaysia. It unites representatives from about 70 NRAs from both ASEAN and OECD member countries and representatives from regional and international organizations. The group first met in 2015 and has since met annually, with an initial focus on good regulatory practice, although this has recently expanded to include quality regulation and sound regulatory governance (OECD 2021a). This is essentially a platform for sharing information and exchanging experiences, although during COVID-19, the initiative went into overdrive to provide as much support as possible to ASEAN NRAs. Indeed, by the end of 2021, the GRPN had met five times since COVID-19 began, “focusing on the changes to regulatory policy making associated with governments’ responses to the pandemic and how better regulation reforms can support recovery” (OECD 2021b, p. 3).
D. ASEAN Member States Embrace Regulatory Agility

Although leaders and policymakers in ASEAN member states recognized how much had been achieved through collaborative processes like the PPWG and JACG, it was still clear that these mechanisms and processes were not viable for the kind of regulatory agility required to combat COVID-19 in the region fully. Accordingly, member states pursued their own solutions for procuring and authorizing different vaccines for their populations. In light of the very different approaches and outcomes that ASEAN represents—in terms of the pooling of national sovereignty and resources (versus the EU’s supranationalism)—Lim (2021) posits that leaders and regulatory bodies in ASEAN took the correct approach for the region.

Indeed, the fact that each ASEAN member state opted for their own responses regarding border closures, lockdowns, physical distancing, and other emergency decisions is a testament to the extreme pressure governments were feeling in the early days of the pandemic. This was compounded by the many unknowns initially surrounding COVID-19 (particularly the nature and transmissibility of the virus) and initial expectations that a vaccine would take years to develop. Add to this the fact that no region-wide emergency pandemic preparedness plan was in place, and the fragility of many member states’ public health systems in their capacity to deal with a national health emergency, and it is no wonder that “urgent socio-political considerations [took] precedence over regional regulatory cooperation” (Lim 2021).

10.5.3 Asia-Pacific Economic Cooperation

APEC’s response to the pandemic was a combination of ministerial summity, joint political declarations, and technical best practices guidelines to support member governments to manage the policy issues that COVID-19 gave rise to. These initiatives span various areas, each with a combination of high-level statements or declarations by ministers or other political leaders, as well as more granular economic and policy analysis intended to guide decision-makers grappling with complex and urgent decisions (APEC 2021b).

A. APEC Life Sciences Innovation Forum

Established in 2002, the APEC Life Sciences Innovation Forum (LSIF) is a multi-stakeholder grouping that unites government, industry, and academia representatives. It has become the leading platform for APEC in health and life sciences. Its mission is threefold: (i) to harmonize with international standards, (ii) to promote technical cooperation with
a view to building capacity, and (iii) to serve as a platform for public–
private collaboration in life sciences innovation (LSIF 2021).

Much of its contribution to regulatory cooperation during the
pandemic was undertaken under the auspices of the APEC Regulatory
Harmonization Steering Committee. Established in 2008 under the
chairmanship of Health Canada, the committee had long been working
toward regulatory convergence for approvals of medical products under
a strategic framework. The target date for completion of this framework
was, coincidentally enough, 2020 (LSIF 2021), with key performance
indicators being adopted by the group in 2018 to measure convergence
across four areas of best practices (Chong, Kim, and Limoli 2021).17

B. APEC Regulatory Responses to Support Vaccine Distribution

APEC has issued targeted policy documents, including the Best
Practice Guidelines for APEC Customs Administrations, to facilitate
the distribution of COVID-19 vaccines and related goods, as well as the
APEC Supply Chain Security Toolkit for Medical Products. The first of
these documents aims to “strengthen the predictability, visibility and
reliability of economies’ vaccine supply chains and also to send a strong
signal to the global community that APEC is committed to expediting
the successful rollout of COVID-19 vaccines” (APEC 2021a). The toolkit,
meanwhile, is aimed at helping policymakers grapple with “areas of
vulnerability in the medical product supply chain and the lifecycle of
medical products,” particularly concerning substandard and falsified
medical products (APEC 2021a). We discuss some of the guidance these
documents provide in section 10.6.

10.5.4 United Nations Economic and Social Commission
for Asia and the Pacific (ESCAP)

Technically part of the United Nations, the Economic and Social
Commission for Asia and the Pacific (ESCAP) is one of several regional
commissions. Like the UN, ESCAP has supported the region in various
ways. For instance, it has developed a “framework to support the socio-
economic response of Asia and the Pacific to the COVID-19 pandemic”

17 These were (i) the removal of the Certificate of Pharmaceutical Product (CPP);
(ii) the use of the Good Manufacturing Practices (GMP) certificate issued
by the Pharmaceutical Inspection Cooperation Scheme (PIC/S) network; (iii) the
management of multiple manufacturing sites under a single license from
the regulatory authority; and (iv) the use of risk-based evaluation based on reliance
practices (Chong Kim, and Limoli 2021, p. 2).
In this framework, ESCAP builds on three main areas of work where it already has the benefit of significant expertise and established policy engagement with its regional members: (i) protecting people and enhancing resilience, (ii) supporting economic recovery, and (iii) restoring supply chains and supporting small and medium-sized enterprises (ESCAP 2020).

10.5.5 PRC Political Summity and Vaccine Diplomacy

The PRC for its part also led a series of initiatives that culminated in several high-level political declarations, as well as a massive program of global vaccine distribution that made a real difference for countries unable to get their hands on sufficient doses of Western vaccines to inoculate their entire populations. The first of these was the Initiative for Belt and Road Partnership on COVID-19 Vaccines Cooperation launched via a high-level political summit in June 2021 that brought together the majority of the Belt and Road countries, comprising (for this initiative) Afghanistan, Bangladesh, Brunei Darussalam, Cambodia, Chile, Colombia, Fiji, Indonesia, Kazakhstan, the Kyrgyz Republic, the Lao People’s Democratic Republic, Malaysia, Maldives, Mongolia, Myanmar, Nepal, Pakistan, the Philippines, the PRC, Saudi Arabia, Singapore, Solomon Islands, Sri Lanka, Tajikistan, Thailand, Turkmenistan, the United Arab Emirates, Uzbekistan, and Viet Nam, who had convened virtually at the Asia and Pacific High-level Conference on Belt and Road Cooperation (Ministry of Foreign Affairs of the PRC 2021a).

Another such declaration, which followed hard on the heels of the first, was the August 2021 Joint Statement of the International Forum on COVID-19 Vaccine Cooperation, which brought together representatives from Argentina, Brazil, Chile, Colombia, the Dominican Republic, Ecuador, Egypt, Hungary, Indonesia, Kenya, Malaysia, Mexico, Morocco, Pakistan, the Philippines, the PRC, Serbia, South Africa, Sri Lanka, Thailand, Türkiye, the United Arab Emirates, and Uzbekistan (Ministry of Foreign Affairs of the PRC 2021b).

Both of these initiatives sought to counter several unfortunate trends that had started to rear their heads as the pandemic got underway in 2020 and vaccines started to be mass-produced in 2021. These included the closing of borders and discriminatory restrictions on travel for nationals from certain countries, as well as vaccine nationalism, which for a while looked like becoming a serious problem as producing countries prioritized the vaccination of their citizens over contractual commitments by vaccine producers to supply different countries with sufficient doses for national vaccination campaigns (Burrow 2021).
Although these declarations are more aspirational than legally binding, they nevertheless furnished the basis for PRC efforts to provide all the countries listed with the necessary means to begin their national vaccine rollouts. They played a significant role in helping contain the virus in developing countries that did not have the financial means to get to the front of the line for more expensive mRNA vaccines that in 2021—at the height of the rollout—were in short supply (Liu, Huang, and Jin 2022).

10.5.6 Regional Initiatives by the World Health Organization

Different regional committees of WHO have long been active in helping their respective constituent governments identify and articulate different public health objectives, including vaccine readiness. For our analysis here, we focus on the most relevant initiatives undertaken by WHO’s Regional Office for South-East Asia and Regional Office for the Western Pacific.

A. Southeast Asia

A Regional Vaccine Action Plan for 2016–2020, published by the WHO Regional Office for South-East Asia, outlines eight goals in the context of the region’s vaccine preparedness, two of which were to prove highly relevant for Southeast Asian governments during the COVID-19 pandemic (WHO 2017). These goals were Goal 7 Introduction of new vaccines and related technologies is accelerated and Goal 8 Access to high quality vaccines is ensured. The first of these goals was originally intended to expand the use of “[new] and increasingly sophisticated vaccines” for “diseases that have not traditionally been targeted by NIPs [national immunization programs]” (WHO 2017, p. 53). At the time, this included hepatitis B-containing vaccines as well as human papillomavirus (HPV) vaccine and pneumococcal conjugate vaccine. However, this program was of considerable strategic value in terms of vaccine preparedness in the context of COVID-19 because of the various activities and the considerable degree of stakeholder coordination that introducing new vaccines requires, including the “involvement of a national technical advisory group in decision-making” and “developing comprehensive plans based on the experience from previous introductions of new vaccines, monitoring uptake of and adverse reactions to the vaccine after introduction and conducting post introduction evaluations” (WHO 2017, p. 54).
B. Western Pacific

The Technical Advisory Group on Universal Health Coverage in the Western Pacific Region was established in 2016 to support governments in member countries to build their analytical, decision-making, and implementation capacity in public health, particularly with a focus on evidence- and people-focused service delivery. During COVID-19, the group proved an essential forum to help governments better understand the pandemic’s threat and evaluate their options in both containing the virus and obtaining and distributing vaccines. In the immediate aftermath of COVID-19 and the gradual reopening of the regional economy, the group has pivoted to, among other things, supporting member country governments “to transform health systems by bringing together data, programmes and systems with UHC as the foundation” (WHO 2023, p. 6) with a focus on “future investments on health system preparedness rather than response” (WHO 2023, p. 11).

10.6 Outlook and Policy Recommendations

10.6.1 Urgency as Driver of Regulatory Agility

Despite its terrible toll, the pandemic has nevertheless proved a boon for the decades-long effort to increase regulatory agility in approving medicines for use and bringing them to market (Lim 2021). Governments felt great urgency, given the health impacts, socioeconomic hardships, and political instability caused by the pandemic. Hence, discovering, approving, and delivering a vaccine was one of the highest political imperatives at the time.

Another important factor was the increased risk tolerance of populations, given the size of unmet needs versus the health and economic risks of COVID-19. This motivated political leaders and regulators to recognize that people were clamoring for a vaccine, both because it promised protection from the health impacts of COVID-19 and because it was seen as the fastest way to end the lockdowns and secure a return to normal economic life. As such, populations were open to new vaccines that lacked the usual long years of extensive clinical trial data.

In many countries in Asia and the Pacific, there was also a distinct lack of regulatory capacity for the independent review and verification of clinical trial data relating to new vaccine candidates by NRAs in the region—and certainly not within the timeframe required to mount an effective response to the unfolding crisis—with the exception of the NRAs of Japan, Singapore, and Australia. As the pandemic wore on, the emergence of new, more transmissible strains forced many, if not
all, NRAs to rely on the tried and trusted emergency authorization procedures of stringent regulatory authorities like the US FDA, the EMA, and WHO itself (Soumyanarayanan et al. 2021).

By 2022, the focus had shifted from regulatory cooperation in approving vaccines to other efforts. These included procuring sufficient quantities of the vaccine, the appropriate time to administer booster shots, the optimum combination of vaccines to improve the efficacy of booster shots against a continuously mutating virus, and improvements to the exchange of information as countries moved to the post-market surveillance stage (e.g., detecting adverse drug reactions). In addition, there was a desire to retain the progress made in regulatory agility during the pandemic, particularly by drug companies and others pushing for greater access to medicines generally.

### 10.6.2 Some Tentative Lessons Learned

The pandemic represented a steep learning curve for political leaders globally, who had to quickly learn to take advice from epidemiologists, virologists, and other specialized medical experts, assisted by health policymakers. Some leaders proved more receptive, while others adhered more to politically expedient solutions or ideological positions.

Despite the high degree of initial uncertainty as to the nature of the virus, countries that swiftly implemented infection prevention and control measures (e.g., border closures, movement restrictions, testing and tracing protocols) were the most successful at avoiding disaster—and rapidly curtailed smaller outbreaks as they occurred. As lockdown fatigue made restrictions on economic activity more politically costly, governments’ measures in the first wave proved insufficient as the virus mutated and sparked successive outbreaks. One upside from the decisions governments had to take during the pandemic is that it instilled in them an appreciation of the cost–benefit calculus involved in imposing lockdowns and other restrictions on socioeconomic interactions and the inherent trade-offs these entail.

Economies that had preexisting outbreak preparedness procedures in place fared better than those without. This was often a function either of an economy’s previous exposure to similar outbreaks (e.g., SARS in 2003 in the PRC; Hong Kong, China; Singapore; and Viet Nam) or other bureaucratically entrenched sensitivities to biosecurity threats (e.g., Australia and New Zealand). Interestingly, the 2019 Global Health Security Index published a report produced after a simulation exercise involving a mock global pandemic that sought to test the pandemic preparedness of about 195 countries. The US and the UK ranked as the most prepared according to this index, a finding that soon proved
misplaced. However, one finding in the Global Health Security Index that proved prescient was the following (Cameron, Nuzzo, and Bell 2019, p. 9):

The GHS Index analysis finds no country is fully prepared for epidemics or pandemics. Collectively, international preparedness is weak. Many countries do not show evidence of the health security capacities and capabilities that are needed to prevent, detect, and respond to significant infectious disease outbreaks.

Undoubtedly, post-COVID-19, world governments will prioritize outbreak preparedness for years to come. Indeed, high pandemic preparedness allowed the PRC, after some initial missteps, to quickly sequence the virus and communicate this information to the world. Likewise, Singapore’s outbreak preparedness and post-SARS protocols allowed it to quickly mobilize and organize effective decision-making at the highest level of political leadership and to deploy a dedicated task force within days of the first reports of the mysterious new virus being detected in Wuhan.

10.6.3 Policy Recommendations to Improve Regulatory Agility

These recommendations aim to support governments and public health authorities in improving the regulatory agility of NRAs, to better ensure the quality, safety, and efficacy of medicines—including, in particular, the “licensing, control and monitoring of the manufacture, import, export, distribution, promotion, and advertising of medicines ... and inspection and surveillance along the entire supply chain” (Ball and Roth 2016).

A. Maintain Publicly Available and Up-to-Date Lists of Approved Medicines

This may be less necessary in countries with a well-regulated and adequately financed public health system. However, transparency deficits still exist in many countries regarding what medicines have been approved for public sale. This can be because of a lack of clear legislative frameworks or regulatory authority to publish such a list. In other cases, such a list may exist, but may not be easily accessible to the public. It also may not be maintained in a format amenable to regular updates.

To address this, public health authorities need to ask several questions, including whether this is something the NRA already does comprehensively or partially and, if this is not being done, why this is
so—i.e., is this due to a lack of legislative and regulatory authority, or resource constraints, or both?

To improve transparency around public health and broader digital transformation initiatives, governments should delegate the authority and allocate the necessary resources to the NRA to establish and maintain such a list. As a starting point, the WHO Model Lists of Essential Medicines can be used for both guidance on what medicines to include in the published national list as well as for how to go about setting up such a list (i.e., what information to provide on and how to catalog different medicines).

B. Mandate Time Limits for National Regulatory Authorities to Adopt and Publish Regulatory Decisions

The long delays in seeking and obtaining regulatory approvals are a common complaint of the pharmaceutical industry. However, this can sometimes be due to issues beyond the NRA’s control, such as the integrity of clinical trial data. In other cases, resource constraints at the NRA are the culprit. This problem can only be fixed with the necessary political will but is also contingent on outside technical assistance and support.

Here, remedying systemic delays begins with asking the right questions: How long does it currently take for the NRA to adopt and publish regulatory decisions in the context of approval procedures? Is that timeframe in line with those required by NRAs in countries at similar levels of economic development? It can also be helpful to ask whether COVID-19 resulted in adopting and publishing regulatory decisions at a more expedited rate than before the pandemic. And if so, what can the NRA do in future to permanently adopt some of the expedited decision-making that it resorted to during the pandemic? The next logical question is, what additional resources or authorizations would the NRA require to adopt such expediencies permanently?

It is suggested that governments study time limits for the adoption and publication of regulatory decisions before and during the pandemic, identifying which innovations the NRA adopted to expedite the approval of COVID-19 vaccines. Governments seeking to institutionalize any such innovations should legislate the adoption of those that can be permanently enacted without compromising the NRA’s core mission, setting binding time limits for NRAs to take and publish regulatory decisions. This also requires appropriating and allocating sufficient resources to support the NRA in this task.

To improve accountability, and to benchmark any progress made, governments should also require that NRAs provide a semiannual accounting of their success or failure in adhering to these new time
limits, with any failures being accompanied by explanations and internal recommendations for how such failures can be avoided in future.

C. Prescribe the Use of the WHO Collaborative Registration Process for Prequalified Products

This is particularly important in countries with NRAs that lack the capacity or resources to manage and interpret complex clinical trial data, or that otherwise struggle to muster the resources required—particularly medical and pharmacological expertise—to oversee and complete lengthy approval procedures. In many countries, the main obstacles to participation are likely to be of a political-economy nature (i.e., existing market participants and entrenched interests are more satisfied with the status quo) and relate to government concerns over the diminution in regulatory sovereignty that joining the procedure may entail. Alternatively, they may be due to resource constraints.

A question to ask is: if an NRA is not already participating, what are the main hurdles to it starting to do so? Governments need to examine whether there would be considerable benefits to stakeholders of the country’s public health sector (consumers, medical practitioners, hospitals, medical insurers) in joining the scheme. If a cost–benefit analysis comes down in favor of joining, then WHO can advise countries on how to do so.

D. Adopt Concrete Steps to Promote Cooperation between National Regulatory Authorities

As noted previously, inter-NRA cooperation is no longer considered desirable in this milieu of complex and fragmented pharmaceutical supply chains but is rather recognized as absolutely essential. The pandemic proved this fact beyond any reasonable doubt. The main challenges lie in garnering sufficient political will from governments and identifying and allocating sufficient resources.

Governments should examine to what extent cooperation between their respective NRA and other more advanced NRAs is already taking place. This cooperation can be either at the regional or multilateral (WHO) level. Governments can examine which NRAs in which countries would be the likeliest and highest-yield partners, considering

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18 Some NRAs in Asia are already participating, e.g., Bangladesh, Bhutan, the Lao People’s Democratic Republic, Malaysia, the Philippines, and Thailand. See WHO web page on accelerated registration of prequalified finished pharmaceutical products at https://extranet.who.int/pqweb/medicines/collaborative-registration-faster-registration.
different forms of cooperation over different time horizons. Partnering with NRAs of similar maturity levels may be desirable.

Next, the government should identify weaknesses in the regulatory capacity of the home NRA that can best be addressed through greater cooperation with foreign NRAs and adopt an action plan to facilitate this. The government seeking to upgrade its own regulatory capacity should approach the foreign NRAs' governments with which greater cooperation is sought and agree upon the terms and conditions subject to which such cooperation shall take place (MOU, MRA, etc.). Governments can also secure and allocate sufficient resources to developing and implementing regulatory cooperation initiatives, if necessary, by approaching relevant donor organizations.

E. Define and Implement a Dedicated Capacity Building Program for the NRA

WHO, among others, has an established track record of capacity building for NRAs in countries like Bangladesh, Rwanda, and Viet Nam. This is first and foremost a resource issue. However, it also involves the challenges of retaining any upgraded capacity over the medium to long term, which is a perennial problem for all capacity-building efforts.

Capacity building should inevitably begin by considering the most cost-effective and impactful way to build capacity in the short to medium term. Further, governments should consider whether this would require large infusions of new resources and qualified staff—and if so, how such resources can be secured (public budget and private sector contributions). Also important from a human resource development perspective is whether short-term resourcing and staffing improvements are sustainable over time, and how to prevent “leakage” of any upgraded human capacity to the private sector or even overseas.

Recommended measures include identifying which weaknesses in capacity are the most amenable to improvement over the short, medium, and long terms. Governments should also identify which capacity-building avenues are likely to be the most impactful and cost-effective (in-house training, staff placements in foreign NRAs, staff secondments from foreign NRAs, etc.). Governments should also identify which foreign NRAs and other institutions can support them in their own NRA’s capacity-building efforts, through institutional twinning programs and similar activities. Finally, governments should consult capacity-building experts in regulatory approval for medicines at organizations like WHO or stringent regulatory authorities, to help formulate and implement its capacity-building program.
10.7 Concluding Remarks

Myriad formal and informal cooperation arrangements allowed scientists, public health officials, regulators, and political leaders globally to unite and work together to combat the coronavirus and restore world health and the global economy. This chapter has focused on how governments cooperated to expedite the approval and rollout of an initial set of vaccines. This was the fastest and most herculean effort to discover, develop, approve, and distribute a new vaccine globally to meet a new virus. It has again proven the resourcefulness and doggedness of the human spirit and what humankind can do when it unites its resources to achieve a common goal.

However, governments did not only cooperate in developing and distributing vaccines. They collaborated across different regulatory areas to exchange information and share experiences on the most effective measures across a range of challenging policy problems related to public health and the equally important goal of protecting the vulnerable from the socioeconomicdeprivations that physical distancing and other infection prevention and control measures entailed.

As the fight against the pandemic continues, governments would be well advised to catalog and internalize the many lessons learned over the past 2 years, to prepare themselves better, their populations, and their economies for future challenges.
References


Innovative Approaches to COVID-19 Vaccine Approvals: Lessons in Regulatory Cooperation and Collaboration

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11 Strengthening Health Systems to Address Inequities in Access to COVID-19 Vaccines in Asia and the Pacific

Valerie Gilbert Ulep

11.1 Introduction

Countries in Asia and the Pacific have been severely affected by the coronavirus disease (COVID-19) pandemic. The economic and health recovery from the pandemic of countries in the region hinges on the rapid and equitable deployment of safe and effective vaccines. As of March 2022, 60% of the population in the region has been fully vaccinated, with a large variation across and within countries. At the same time, vaccination coverage in high-income countries in the region was 80% compared to 10% in low-income countries. Booster shots are being administered in some countries, while poorer countries have yet to achieve their coverage targets for the primary series. For example, Singapore has already vaccinated 68% of its population and the Republic of Korea 62%.

Equitable distribution of COVID-19 vaccines means that all countries should have access, regardless of economic development (WHO 2020a). Vaccine inequity is a serious threat to public health and the global economy. Allowing the populations of certain countries to remain unprotected increases the risk of continuous viral transmission and mutation, leading to a patchy economic recovery (Asundi, O’Leary, and Bhadelia 2021). The problem of accessing lifesaving vaccines and drugs in developing countries has been observed in previous public health emergencies and epidemics (e.g., influenza outbreaks in 2004 and 2009) (Fidler 2010). With the COVID-19 pandemic, a concerted effort has been made to address the problem by creating the COVID-19
Vaccines Global Access initiative called COVAX (WHO 2020b; Emanuel et al. 2021). Despite this effort, vaccine inequity remains a challenge in many countries in the region (Stein 2021). Poor subnational states and disadvantaged populations generally have lower vaccination coverage (Thankur et al. 2020; Marmot et al. 2020).

The unequal distribution of COVID-19 vaccines across and within countries in the region during the initial year of vaccine rollout could be attributed to vaccine nationalism, characterized by competition between countries for the procurement of vaccines (Katz et al. 2021). However, as COVID-19 vaccines become part of the disease prevention programs of each country and as global supply stabilizes, the readiness of the national health systems becomes even more critical (Haldane, De Foo, and Abdalla 2021).

11.2 The State of the COVID-19 Pandemic in Asia and the Pacific

As of March 2022, there were 137 million confirmed cases in the region and 1.4 million deaths, with significant differences across countries. Figure 11.1 shows the large variation in reported COVID-19 deaths relative to the population in selected countries of the region (Ritchie, Mathieu, and Rodés-Guirao 2020).
Mathieu, and Rodés-Guira 2020). However, many cases have gone undetected and are excluded from official death tallies. Figure 11.2 shows that excess mortality is significantly higher than reported deaths in some countries in the region. Excess mortality is a comprehensive measure of the impact of the pandemic on mortality. It includes the confirmed COVID-19 death count, COVID-19 deaths that were not diagnosed, and deaths indirectly attributed to the pandemic, such as the deaths of people who were unable to access treatment owing to the pandemic’s impact on health-care systems (Ritchie, Mathieu, and Rodés-Guira 2020; David 2022).

The disease burden attributed to COVID-19 has significant variance across populations. The pandemic has disproportionately impacted older people and people with chronic underlying conditions. The mean age of people dying of COVID-19 is 70 years, and populations with chronic conditions are 1.5 times more likely to die (Simonsen and Viboud 2021; Popkin et al. 2020). Figure 11.3 uses regression to illustrate the linear relationship between cumulative COVID-19 mortality (death
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per million population, as of March 2022) and the percentage of the population aged 65 years and older. However, emerging studies have shown that this linear relationship was only significant for countries with low hospital beds, and the number of hospital beds indicates health-care system capacity (Farzanegan 2020).

Figure 11.3: Age Structure of Confirmed COVID-19 Deaths in Countries in Asia and the Pacific and Other Regions, March 2022

COVID-19 = coronavirus disease.

Note: Blue dots represent countries in Asia and the Pacific, and light blue dots represent countries in other regions.

Source: Ritchie, Mathieu, and Rodés-Guira (2020).

Structural inequities exacerbate the variation in disease burden across populations. Vulnerable populations such as minority ethnic groups, people living in higher socioeconomic deprivation, and other marginalized groups have a greater risk of COVID-19 infection. They have higher rates of almost all known underlying clinical risk factors that increase the severity and mortality of COVID-19 (Bambra et al. 2020). The inequities caused by the pandemic are observed worldwide, including in Asia and the Pacific. For example, foreign workers in Singapore, Malaysia, and Thailand were at a higher risk of infection.
Manual labor foreign workers in Singapore who live in crowded dormitories fueled the first wave of infection in the country (Collins and Low 2021). This is an example of how crowded conditions result in the rapid spread of infection. Similar patterns were observed in urban slums or informal settlements in Bangladesh, India, and the Philippines (George et al. 2021; Sahasranaman and Jensen 2021).

Almost all countries in Asia and the Pacific have implemented public health interventions to stop the exponential spread of infection, such as mobility restrictions, school and business closures, and border controls. However, the duration and stringency of interventions vary across countries. Some countries maintained high stringency throughout the pandemic (e.g., Bangladesh and the Philippines). For a long time, the People’s Republic of China (PRC) has adopted a “zero-COVID” policy, which refers to its approach to controlling the spread of disease within its borders. The policy involves aggressive measures to prevent new outbreaks, including strict border controls, mass testing, and contact tracing. However, these stringent mobility restrictions came with a heavy price, causing unprecedented economic recessions in many countries (Reuters 2021). The regional economy of Asia and the Pacific shrunk by approximately 3.8% in 2020 (ESCAP 2021).

Governments in the region rolled out massive vaccination campaigns as soon as vaccines became available. The development of safe and effective COVID-19 vaccines has dramatically changed the course of addressing the pandemic. Most countries in Asia and the Pacific started their COVID-19 vaccination campaigns around the first quarter of 2021, 1 to 2 months after countries in North America and Europe. Many countries in the region aimed to vaccinate at least 70% of their population to achieve high population protection. The World Health Organization (WHO) set a target for COVID-19 vaccination to reach at least 40% of the global population by 2021 and 70% by 2022 (WHO 2021b). Given the tight global supply of vaccines, particularly during the first few months of the vaccination campaigns, priority was assigned to selected population groups such as health workers and older people (considered the most at risk of morbidity and death). Countries that received COVID-19 vaccine donations from COVAX are also mandated to follow the prioritization framework. The COVID-19 vaccine universal rollout (to the rest of the population) commenced asynchronously across countries in the region. In Singapore, for example, universal vaccination began in April and May 2020, while in low- and middle-income countries (Bangladesh, Indonesia, and the Philippines), it began in August and September 2021 (Hale et al. 2020).
11.3 Equitable COVID-19 Vaccination in Asia and the Pacific

Vaccine equity is critical in addressing the pandemic. Rapid and equitable distribution of diagnostics, therapeutics, and vaccines within and across countries is the most effective way to address the health and economic impact of COVID-19. Strategies that ignore equity undermine the effectiveness of vaccination as a tool to control the pandemic, potentially increasing hospitalizations and deaths and delaying economic recovery (Asundi, O’Leary, and Bhadelia 2021). Inequitable vaccine distribution leaves millions of people vulnerable to the virus and allows variants to emerge and reverberate across the world. Globally, the pandemic’s negative consequences will include unequal economic growth impacts.

Approximately 60% of the population of Asia and the Pacific had been fully vaccinated as of March 2022. Vaccine coverage in the region is highly unequal. For example, coverage in Singapore has already reached 90% compared to less than 10% in Afghanistan. Figure 11.4 shows the

Figure 11.4: COVID-19 Vaccine Coverage and Gross National Income per Capita, Selected Countries in Asia and the Pacific, March 2022 (%)


Source: Author’s data analysis from Oxford University and World Development Indicators.
positive relationship between vaccine coverage (fully vaccinated) and income per capita. Most countries that have already reached a coverage of 70% are high-income countries (e.g., Australia, Singapore, New Zealand, and Japan). Several low- and middle-income countries demonstrate high vaccine coverage, such as Cambodia and Bhutan (Ritchie, Mathieu, and Rodés-Guíra 2020). A similar pattern can be observed for booster coverage. Coverage could be affected by the share of priority population; countries with a larger share of older people (e.g., Japan) tend to have higher coverage relative to countries with younger population groups. As of March 2022, most countries in the region have already rolled out the COVID-19 vaccination program to children (aged 5–17 years), except Afghanistan, Nepal, Papua New Guinea, and Solomon Islands. Figure 11.5 shows that the high-income countries in the region were more able to vaccinate their population than low- and middle-income countries.
Emerging data show a significant disparity in vaccine coverage within countries. Determining the magnitude of inequality within countries is difficult as comprehensive databases remain limited. However, available subnational coverage data suggest wide disparity, especially in developing countries. Figure 11.6 shows the difference between the highest and lowest coverage rates for selected countries in Asia and Pacific with available subnational data (e.g., region, state, province, prefecture). Within-country inequality tends to be higher in low- and middle-income countries compared to high-income countries. In some provinces and states in Indonesia and India, coverage has already reached 70%–100%, while other subnational units have yet to reach 20%. In contrast, there is little disparity between the highest and the lowest subnational coverage rates in high-income countries such as Australia, New Zealand, and Japan (IMF 2021a).

**Figure 11.6: Absolute Difference between the Highest and Lowest Coverage of Subnational Units, March 2022 (%)**

Note: Absolute difference = highest coverage – lowest coverage.

Source: Author’s analysis of data from the International Monetary Fund.
The supply of COVID-19 vaccines varies across countries in the region. Based on publicly available data, Figure 11.7 shows secured COVID-19 vaccines relative to the population of countries in Asia and the Pacific. High-income countries in the region, such as Australia, New Zealand, and Japan, have already secured vaccine supply 5–10 times greater than their population size, while a large portion of the population of some low- and middle-income countries is not yet vaccinated, and the quantity of secured vaccine is lower than the population size. Figure 11.8 shows the variation in sources of secured vaccines in the region. Many island countries have relied exclusively on COVAX and bilateral donations in expanding coverage. Interestingly, sources of secured vaccines in Southeast Asian countries include COVAX and bilateral deals.

Figure 11.7: Secured COVID-19 Vaccine and Vaccine Coverage Rate, March 2022 (%)
Vaccine supply does not automatically lead to vaccination. Even if enough vaccine doses are eventually made available through various channels, success will be hampered by challenges in the health systems in developing countries. Figure 11.9 shows that the share of administered vaccines out of delivered vaccines varies across countries in the region. This suggests the low absorptive capacity of some countries (OECD 2021). The high number of vaccines that were not administered could reflect challenges in the health systems to allocate and administer the vaccine with speed and agility, particularly because of limited infrastructure and human resources. Demand-side challenges could also contribute to the low uptake of vaccines.
Vaccine equity should reflect policies and strategies to ensure equal access across countries and to address structural inequities that prohibit disadvantaged population groups (e.g., poor people, older persons, persons with disabilities, indigenous people, migrants, women, prisoners) from accessing vaccines (Agarwal et al. 2021). Disadvantaged groups, such as migrants, indigenous peoples, women, and the poor, are less likely to access essential health services (Smith and Kaluzny 1974). There is a lack of comprehensive data to examine the association between structural inequities in vaccine coverage. However, the best available global data and case studies provide evidence of inequities. For instance, as of December 2021, coverage in Bangkok had reached 100%. However, coverage in the provinces of Thailand near international borders (e.g., Cambodia, Malaysia, the Lao People’s Democratic Republic, and Myanmar), which are
epicenters of cross-border migration, was approximately 30%–40% (WHO 2021c). In the Philippines, the socioeconomic gradient in vaccine coverage is extremely wide. In Indonesia, the coverage rates in Papua and Maluku, islands of mostly indigenous people, were only 20% and 40%, respectively (as of December 2021), in contrast to the reported 140% in the megacity Jakarta (IMF 2021a). Geographic barriers pose challenges to vaccine access, for example, in high altitude landscapes of the Himalayan regions and Afghanistan, Bhutan, Nepal, and Pakistan, or remote areas with war, instability, and conflict (Acharya, Ghimire, and Subramanya 2021). Megacities in the Philippines have already reached 90% coverage. Still, coverage was only 10% in the poverty-stricken and war-torn Bangsamoro Autonomous Region in Muslim Mindanao (as of December 2021) (Department of Health of the Philippines 2021).

Countries have adopted allocation frameworks to promote vaccine equity. Given the limited COVID-19 vaccine supplies and resources to vaccinate the population, almost all countries adopted vaccine allocation frameworks upholding utilitarian principles by prioritizing the population that maximizes the best health outcomes, in this case, older people and people with co-morbidities. However, other countries (e.g., Indonesia) took a divergent path by prioritizing economic workers over older people (Witando and Diela 2021). Several countries have included egalitarian approaches in their vaccine allocation framework. For example, in the Philippines and India, priority was given to slum dwellers and people living below the poverty line (Basu and Mishra 2020; Department of Health of the Philippines 2020). However, the adherence to and implementation of these utilitarian and egalitarian frameworks should be examined as leakages and elite capture are reported to be rampant. For instance, in the Philippines, the vaccine coverage of all-adult populations in megacities has already reached 90%. However, nationwide coverage for older people, despite being a priority group, remains at 50% (as of December 2021) (Department of Health of the Philippines 2021).

In addition to supply challenges, demand-side challenges such as vaccine hesitancy could drive low vaccine coverage in some countries. Figure 11.10 shows the share of the population willing to be vaccinated if the supply is available. Willingness is high in most countries in Asia and the Pacific. Still, others have remarkably low levels of willingness, such as Afghanistan, Fiji, Mongolia, the Russian Federation, Solomon Islands, and Papua New Guinea. Low willingness in some countries is largely driven by the spread of conspiracies and misinformation and a growing anti-vaccination sentiment (Forman et al. 2021; Carrieri, Madio, and Principe 2019). Around 30% of online information in Asia and the Pacific could be more reliable (Collective Service 2022). Digitalization
could facilitate vaccine demand, as vaccination drives in many countries have depended on digital platforms (e.g., electronic booking systems and demand generation). The large digital divide could exacerbate the problem of lack of access within and across countries in the region. Rural populations and those lacking digital literacy have been included in new vaccination processes in some settings, while only the privileged, educated, and urban populations have benefited (Poole, Ramasawmy, and Banerjee 2021).

11.4 Drivers of Inequity in Vaccine Access

As COVID-19 becomes part of most countries’ prevention and control programs, equitable access will be highly dependent on the capacity and readiness of health systems (Usher 2021). In this section, we classify three supply-side barriers that could impede equitable vaccine access: financial, geographic, and regulatory. Financial access means there are few direct or indirect cost barriers to receiving the vaccine. These access factors are
adapted from a framework developed by the Harvard University Health and Places Initiative (2014), which identified different types of health-care access. Geographic access means the absence of barriers, including distance, transportation, and other physical challenges. Regulatory access means the absence of unnecessary policies or processes impeding timely vaccine access. These supply-side barriers in the health system are not new. They are long-standing features of inequitable access to essential health-care services and goods. Figure 11.11 shows the strong linear relationship of the universal health coverage service coverage index and COVID-19 vaccine coverage as of December 2021. The service coverage index measures the capacity of health systems to provide a wide range of essential health-care services to the population (World Health Organization 2019). Figure 11.12 shows the positive correlation between DPT3 (three doses of the combined diphtheria, tetanus toxoid, and pertussis vaccine) vaccination and COVID-19 vaccine coverage. In general, low coverage of routine childhood vaccination is a marker of a challenged health system.

Figure 11.11: Coverage of COVID-19 Vaccines and Universal Health Coverage Service Coverage Index, March 2022

COVID-19 = coronavirus disease.

Note: Blue dots represent countries in Asia and the Pacific.

Source: Author’s analysis of data from the World Health Organization and Oxford University.
11.4.1 Financial Access

Financial barriers reflect challenges in countries’ health financing systems. Financial access is one of the determinants of health-care utilization. We must examine financial access from a health financing perspective to understand financial access. One of the core functions of any health financing system is to mobilize resources from public sources (e.g., government revenues, social insurance) or private sources (e.g., private insurance and out-of-pocket or user fees)—but the level and source of financing matter. Essential vaccination programs such as routine childhood immunization should be publicly financed and out-of-pocket (OOP) costs discouraged. WHO and multilateral organizations have discouraged OOP costs or user fees because it is counterproductive to the goals of vaccination programs (WHO 2018). Solid evidence indicates that OOP costs in developing countries discourage vulnerable populations from seeking vaccination.
OOP costs remain the major source of health financing in the region. In 2018, OOP costs accounted for about 57% of total health spending among the region’s low- and middle-income countries compared to 22% among high-income countries (WHO 2021a). Public spending on health remains relatively low, with marked differences across countries in the region. With the enormous socioeconomic impact and political pressures of COVID-19, governments have mobilized public resources (e.g., either from general revenues or external sources) to finance the pandemic response, including vaccination programs. However, important policy questions remain: Will governments sustainably allocate higher public spending to finance COVID-19 vaccines as with any other regular prevention and control program? Will governments rely on OOP costs to finance some of the vaccination programs? Will governments allow the private market to administer COVID-19 vaccines parallel to the public system, financed through OOP costs? Current vaccines can be sold in the market, which is the delivery structure of vaccines in countries such as India and the Philippines (Ulep and Uy 2020). Since financial pressures are coming when many economies are in crisis due to the pandemic, governments may have to use OOP costs to mobilize incremental resources for health services. OOP costs could provide adequate, timely, and reliable vaccine resources, thus contributing to the overall financial balance. However, the potential benefits of using OOP costs to sustain the COVID-19 vaccination program would not offset the negative effects on equity. Challenges to raising public resources for COVID-19 vaccines are mounting, given the enormous financing needs of the program. In low- and middle-income countries, the cost of vaccinating 40% of the population accounts for approximately 10%–20% of total national health spending. Figure 11.14 shows the resources needed to fund the COVID-19 vaccination program for 40% of the population compared to routine immunization.

Fiscal decentralization could exacerbate vaccine inequity within countries. Public financing in general should promote equitable access to vaccination. However, the growing trend toward political and fiscal decentralization (e.g., in India, Indonesia, the Philippines, and Viet Nam) should prompt governments to examine the financing capacity and decision-making process of subnational units; otherwise, it will have a tremendous impact on vaccine equity. While empirical evidence suggests a variable impact of fiscal decentralization on vaccination coverage (Khalegian 2004), heavy reliance on subnational financing for vaccination programs could have a detrimental equity implication. In general, the subnational units with the lowest capacity to finance the vaccination program are also in need, and where health services are relatively costlier to implement because of geographic and supply-side constraints. Yoong (2007) examined the impact of decentralization
Figure 11.13: COVID-19 Vaccination Program as a Share of Health Spending, March 2022 (%)

COVID-19 = coronavirus disease.
Note: Blue dots represent countries in Asia and the Pacific.
Source: Author’s data analysis from the United Nations Development Programme and the World Bank.

Figure 11.14: Cost of Routine and COVID-19 Vaccination Program as a Share of Gross Domestic Product (%)

Source: Author’s data analysis from the United Nations Development Programme and WHO.
in Madhya Pradesh, one of India’s largest and poorest states. Decentralization led to a fall in immunization coverage, particularly in rural areas. Maharani and Tampubolon (2014) suggest that fiscal decentralization in Indonesia did not impact childhood immunization. They conclude that decentralization could have improved outcomes for childhood immunization due to limited local capacity in planning, budget development, and budget execution. A similar pattern was observed in the Philippines. While routine vaccines are procured directly by the central government through the Department of Health, local government units finance operational costs (e.g., syringe, and health promotion campaigns). However, given the limited capacity of some local government units to finance and deliver programs, decentralization resulted in disparities in vaccine coverage (Ulep and Uy 2020). In some settings, where taxes levied at the subnational level are often less progressive than national-level taxes, decentralization led to inequitable public financing. The rich population mostly benefited from the public vaccination program.

Reports show emerging signs of marked COVID-19 vaccine inequity in decentralized regimes. For example, the provinces of Viet Nam have a greater role in financing immunization and are responsible for financing the operational costs of the COVID-19 vaccine rollout. While subnational autonomy has created flexibility and efficiency in vaccine operations, funds were inadequate in some provinces. In contrast, Pakistan recentralized vaccine procurement and financing to improve efficiency (Learning Network for Countries in Transition 2021, p. 8). In the Philippines, the global supply was limited during the early stages of the COVID-19 vaccination campaign. Affluent local government units in the country (mostly in megacities) purchased their own COVID-19 vaccines, leaving relatively poor local government units to rely on nationally procured vaccines—such a scenario created inequality in vaccine coverage and political tensions within the government (Cabico 2021). Decentralization has been the subject of debates on the roles of subnational units during the height of the pandemic, not only during the rollout of vaccination programs (OECD 2020). Previous studies have challenged the effectiveness of decentralization in addressing the pandemic. Cheng, Li, and Zhang (2021) find that COVID-19 spreads faster in decentralized countries, leading to a higher disease burden.

11.4.2 Geographic Access

Geographic access refers to the supply, diversity and distribution, and physical accessibility of health-care services (Health and Places Initiative 2014). In identifying geographic barriers to vaccine access, starting with the readiness of primary care systems is imperative.
Primary care is the locus of sustainable implementation of COVID-19 vaccination, as with any preventive intervention. Hence, any challenge in vaccine equity could reflect weaknesses in primary care. Under geographic access, three supply-side elements are discussed: health workers, health facilities, and supply chains and logistics.

All countries need a sizable health workforce to meet the demands of the COVID-19 vaccine rollout. Health workers should be widely available to reach the vaccine coverage targets in all parts of a country, including far-flung areas. While almost all countries, even those with resilient health systems, faced a scarcity of vaccinators, it is apparent in low- and middle-income countries where shortage and maldistribution have been a chronic problem. Figure 11.15 shows the large variation of nurses and midwives per 100,000 population in selected countries in the region. The within-country disparity is also ubiquitous. For example, poor provinces in the Philippines suffer from a shortage of health workers, as most are in cities (Abrigo and Ortiz 2019). This shortage of health workers has implications for the quick deployment of vaccines, particularly in far-flung areas.

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**Figure 11.15: Health Worker Density of Selected Countries in Asia and the Pacific**

Nurses and midwives per 100,000 population

PRC = People’s Republic of China.

The need for more trained human resources to perform and assist the COVID-19 vaccination program is a common problem. Training more health workers will ensure that vaccines are administered to all, including those in poor and hard-to-reach communities. Also, it will ensure that vaccines are delivered safely. The lack of trained health workers compromises vaccine throughput and the program’s quality, safety, and efficiency. In many countries, vaccines are routinely administered to children, but the massive volume of people needing COVID-19 vaccination—this time, mostly adults—requires a different skill set. Based on the WHO Joint Reporting Form, the percentage of countries reporting at least one adult vaccination program ranged from approximately 10% in Southeast Asia to 90% in Europe. Successful delivery of COVID-19 vaccines could be derailed by the lack of sufficient adult immunization infrastructure (Williams et al. 2021). The lack of training led to a wastage of vaccines. For example, the Government of India attributed high wastage to health workers’ lack of proper training in using multidose vials and improper planning at the local vaccination centers (Kaunian 2021). In Afghanistan, only 10% of vaccinators fulfilled the required educational criteria, and only 14% of health facilities have vaccination micro plans, which are comprehensive guides for health workers in all aspects of the vaccination program (Wardak et al. 2021).

The scarcity and maldistribution of health workers could disrupt the delivery of other primary care services. In assessing vaccine access from a health human resources perspective, we must examine the vaccination program with other primary care services and programs that health workers should provide. Even before the pandemic, many health workers were overworked—and the pandemic has exacerbated this problem. In addition to the COVID-19 vaccination program, health workers still need to maintain the delivery of essential routine vaccinations, manage potential COVID-19 cases, perform surveillance of other diseases, and provide health promotion services. Since the onset of the pandemic, many national immunization programs against diseases such as diphtheria, measles, and poliomyelitis have been substantially disrupted in at least 68 countries, not only in the region but globally, affecting up to 80 million children (WHO 2022c). Many countries in the region have high turnover rates of frontline health workers because of the high levels of physical and mental stress induced by the workload and the risk of infection (delos Santos and Labrague 2021; Yousaf, Nasani, and Haffar 2021; Sethi et al. 2020). The high turnover rates among

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1 The Joint Reporting Form collects countries’ annual immunization data, which help identify trends and gaps at the country, regional, and global level. The data are also used for informing progress toward the Immunization Agenda 2030.
community health workers, in particular, compromise the quality and quantity of vaccination programs, especially in far-flung communities where health workers are scarce. However, governments in the region have developed programs to address this problem. In the PRC and Pakistan, for example, the government raised the morale of frontline health workers by providing financial support and acknowledging their services—and this was reported to have psychological benefits (Noreen et al. 2020).

Studies have identified low remuneration and incentives as reasons for the high turnover of health workers, especially in geographically challenged areas. Monetary remuneration and nonmonetary incentives are important for maintaining motivation and minimizing attrition. With a more harmonized approach to setting remuneration and incentives for health workers, their performance may be consistent, affecting health outcomes (Bezbaruah et al. 2021).

Regulatory barriers prevent countries from expanding their pool of potential vaccinators. Existing medical regulations and policies prohibit certain cadres from administering vaccines. Task shifting and rationalization of health workers can help to address scarcity and redistribute health workers in low- and middle-income countries. In response to COVID-19, high-income countries revised their policies to allow certain health cadres to administer vaccines. For example, the Government of the United States authorized pharmacists to procure and administer COVID-19 vaccines. Several states have considered expanding their scope of practice or licensure of nontraditional providers, such as advanced emergency medical technicians, paramedics, and medical and nursing students, for COVID-19 vaccine administration.

The COVID-19 crisis has revealed the fragility of supply chain systems. Vaccines were developed with unprecedented speed. A critical concern now is whether it will be possible for the pharmaceutical supply chains in each country to scale up and deploy vaccines with speed and agility. Supply chains move medical goods from manufacturers to the point of use (e.g., primary care facilities) through many distribution layers using different modes of transport and storage. Hence, well-functioning and efficient supply chains are critical for successful vaccination programs. Even before the pandemic, underperforming pharmaceutical supply chains were a major challenge, especially in low- and middle-income countries. In most developing countries, supply chains are complex and fragmented, with multiple configurations, levels of maturity and performance, and degrees of private sector participation. The
COVID-19 vaccines have the added complexity of requiring cold chain logistics and more agility and efficiency to preserve product quality and availability. Some COVID-19 vaccines are temperature sensitive. The inability to maintain the recommended temperature may reduce the efficacy of vaccines, especially in tropical regions. About 20% of vaccination facilities in low-income countries do not have cold chain capacity, and a 2017 review by Gavi, the Vaccine Alliance found that 37%–50% of vaccines in low- and middle-income countries had been stored at incorrect temperatures, which undermined the efficacy of vaccines (Gavi 2022). Supply chains are also more difficult to manage in countries with geographic challenges and areas prone to natural hazards. Governments operate supply chains in environments with suboptimal communication and imperfect information (Quiros and Alam 2021).

### 11.4.3 Regulatory Access

Regulatory access means the absence of unnecessary policies or processes impeding timely vaccine access. During an emergency, one of the major regulatory constraints, particularly in developing countries, is the ability to assess information. The ability to expediently issue emergency authorization for a vaccine during a pandemic may depend on local capacity and willingness to “benchmark” alongside stringent regulatory authorities, recognizing that WHO takes more time to issue an authorization. Manufacturers file applications for emergency authorization with different levels of urgency in different countries.

In the medium to long term, developing countries must be able to produce vaccines locally. However, intellectual property rights are regularly cited as a constraint to scaling up vaccine access in developing countries (OECD 2020). Sharing technical knowledge, expertise, and know-how is increasingly seen as a challenge. More importantly, developing countries need strong regulatory authorities to manufacture products that meet global standards. Unfortunately, WHO estimates that only one out of three countries can effectively regulate domestic manufacturing of medical products, expanding vaccine manufacturing without guaranteeing adequate regulatory capacity would have detrimental repercussions on the quality and safety of the product—and this certainly would damage public trust in vaccines (Guzman and Yadav 2021). According to the latest data from WHO (2022a), vaccine-producing countries in the region with functional national regulatory authorities are India, Indonesia, Japan, the PRC, and the Republic of Korea.
11.5 Recommendations to Governments

Even if vaccine supply were sufficient for all countries, health system constraints would make it difficult to roll out COVID-19 vaccines. Hence, our recommendations revolve around strengthening health systems.

(i) **Accelerate universal health coverage.** Constraints and inequitable access to COVID-19 vaccines manifest problems in health systems. Even the Access to COVID-19 Tools (ACT) Accelerator, a new and groundbreaking global collaboration led by WHO to fast-track the development and production of COVID-19 vaccines, and equitable access to them, has recognized the importance health systems strengthening as a critical pillar, albeit with less focus and funding than other pillars. Addressing the problem holistically at the systems level will address challenges not only in the vaccination program, but also in other public health programs. Therefore, governments should focus on the following reform areas:

(a) **Expand primary care.** Preventive and existing programs, including vaccination programs (both COVID-19 and non-COVID-19) are typically provided at the primary care level. Hence, governments should make it a priority to improve the quality and availability of primary care. This includes expanding capital investments and health benefit packages for primary care services.

(b) **Increase public financing.** The move to universal health coverage means increasing pooled public financing: government budget, social insurance, and external grants and aid. Governments should aim to reduce the role of private financing mechanisms, particularly OOP costs, to fund critical and cost-effective public health programs, such as vaccination for high-burden diseases. However, given the limited fiscal space for health, governments should mobilize domestic resources through innovative means to fund public health programs (e.g., health earmarking).

(c) **Prioritize populations in fragile contexts.** Vulnerable populations, such as women, indigenous peoples, poor households, and migrants, are less likely to seek health care, including vaccination, because of geographic, structural, and institutional barriers. Hence, governments should develop innovative financial and delivery mechanisms to increase access among vulnerable groups.
(ii) **Institute genuine reforms in the health information system.**

The COVID-19 pandemic has provided an opportunity to reflect on the innovations that should become part of an enhanced health information system in the future. Governments should adopt a health information system to facilitate health access (front-facing) through telehealth systems and to improve business operations of health facilities, as well as supply and logistics (back-end).

Before the COVID-19 pandemic, health-care services were traditionally provided through in-person interactions. The spread of the pandemic created an urgent need for health-care providers to deliver services using digital platforms. Governments may need to institute reforms to ensure the quality of care (e.g., telemedicine should be included in medical curricula, and providers should receive training) and the financial sustainability of telemedicine (e.g., by including it in government health benefits packages).

Digital technology can improve business operations. In developing countries, medical records in health facilities are kept manually and must be interoperable. Governments should implement an electronic medical record system to improve the efficiency and accuracy of health data. Information is critical in the movement of goods and services. Information is a key supply chain driver because it allows other systems to create an integrated supply chain at different ecosystem levels. Information is crucial to supply chain performance because it provides critical insights to decision-makers. With information, they would know what providers want, how much inventory is in stock, and when more products should be produced or shipped.
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12

Insights and Recommendations

Rupa Chanda, Pralok Gupta, and Matthias Helble

12.1 Overview of Key Points

Vaccines play a vital role in public health. This becomes clear when looking at the numerous national immunization programs around the world. And, as this book reveals, vaccine production and distribution are part of a complex “from lab to jab” process. It involves many steps: starting from research and development (R&D), related financing, and technology transfer arrangements through the supply chains and related flows to ensure essential inputs are available for vaccine production, the distribution of the produced vaccines across borders through trade, transport, and logistics, and finally to the distribution and administration of vaccines within countries as shaped by their national health system capacity. This complexity is also reflected in the wide range of players, regulations, and policies involved in the end-to-end cycle for vaccines. The discussion in this book further highlights the vulnerability and risks associated with overdependence on a few countries for the supply of essential vaccines and their inputs, as the coronavirus disease (COVID-19) pandemic made evident, and therefore the need to disperse production capacity across more countries as well as address the bottlenecks and regulatory hurdles that today stifle vaccine development and timely and efficient distribution.

A key message of this book is that if the aim is to make access to vaccines more affordable and equitable, then vaccines must be seen as global public goods that are critical for ensuring global health security. Like all public goods, therefore, their financing, R&D, production, and distribution will require a combination of unilateral, regional, and multilateral measures, as well as collective action in terms of regulatory coordination and cooperation among countries across the many facets of the vaccine cycle, from inception to delivery.
12.2 Key Recommendations

The discussion that follows summarizes the key insights and policy approaches put forward in this book. These are presented under three broad clusters: (i) the development of vaccines, (ii) the cross-border delivery of vaccines, and (iii) the national distribution of vaccines. We also provide some observations on how some of the proposed recommendations could be taken forward and areas for further research and analysis.

12.2.1 Vaccine Development

The initial chapters provide an overview of the economics, actors, and key requirements involved in vaccine R&D, which constitutes the very first stage of the vaccine life cycle. The discussion notes the role individual governments can play, such as through advance purchase commitments, public investments, and various other push and pull mechanisms to incentivize vaccine development and mitigate the risks involved. Beyond the national strategies, however, the discussion stresses the importance of collective measures to address various dimensions of vaccine development. For instance, in the context of vaccine R&D financing, a prerequisite for vaccine R&D, the discussion highlights the need for global and regional cooperation for prioritizing vaccine development based on collectively agreed criteria, such as disease prevalence and burden, the potential for epidemic and pandemic spread, R&D capacity, and financial viability. Also of importance are cooperation mechanisms involving governments, industry, academia, and international and regional organizations to address other aspects of vaccine development. These include facilitating the sharing of data and technology, ensuring continuity in funding of priority vaccine candidates and platforms, undertaking needs assessments, promoting capacity building, and forging collaborative partnerships between universities, research institutes, and industry across countries to promote joint research projects and exchange.

The chapters specifically highlight the scope for regional and subregional efforts in Asia and the Pacific through relevant organizations. These efforts could be directed toward mapping regional needs and identifying financing gaps, devising regional strategies for vaccine research in collaboration with regional partner institutions (e.g., World Health Organization [WHO] regional offices) and other stakeholders, and establishing a regional vaccine research network that enables the sharing of data and knowledge. This network could also serve as a platform for conducting advocacy,
coordinating initiatives, undertaking joint projects, and determining region-wide research priorities. The region could also embark on initiatives to mobilize resources for financing vaccine R&D. These regional initiatives could include creating a regional financing facility that finances joint research projects and prevents overlaps in R&D funding. It could take the form of a regional mechanism based on earmarked voluntary contributions by governments and philanthropic organizations or a region-wide airline ticket levy to fund regional vaccine R&D. Such regional financing facilities could work along the lines of global schemes such as Gavi, the Vaccine Alliance or the Global Fund by earmarking funds to support global public goods for health. These regional efforts could also be supported by multilateral, regional, and other development finance institutions.

Another proposed area for regional action is pooled procurement. Modeled after the proposed mechanism by the Center for Global Development, all countries affected by a common disease in the region could pool their market-driven, value-based advance commitment to purchase new vaccines. This would provide pharmaceutical companies a guaranteed market for newly developed vaccines. Such a pooled commitment at the regional level could incentivize vaccine R&D by reducing uncertainties about demand and serve as a coordination platform to prioritize R&D in vaccines and make investment decisions more predictable and transparent.

The first set of chapters also addresses the issue of managing intellectual property (IP) rights, which are an integral part of any vaccine R&D process. The key point that emerges in managing IP for vaccine R&D is that countries need to strengthen analytical and technical capacity to effectively administer and comply with IP legislation. At the same time, collective efforts with regional partners and institutions are needed to track technologies, undertake IP mapping exercises, promote synergies, encourage mutual learning, and exchange best practices.

In sum, the discussion on the initial stages of the vaccine life cycle outlines the scope for promoting vaccine R&D through a combination of national, regional, and global efforts. These efforts need to be directed at financing, procurement, needs analysis, capacity building, and technology transfer. The main message is that vaccine R&D, though it often seems like a private sector affair that pharmaceutical companies lead, in reality is a global public good. Individual country-level efforts can yield global benefits, but given the complexities involved in vaccine development, global and regional coordination mechanisms and platforms are also needed. Furthermore, there needs to be coherence between these national and collective strategies.
12.2.2 Cross-Border Delivery

The next set of chapters address the cross-border movement of vaccines, involving trade, transport, and logistics and the related regulatory and legal arrangements that facilitate these flows. Several important insights emerge from the discussion.

On the trade front, the discussion calls for countries to review and eliminate tariffs on vaccines and related products to reduce the cost of importing vaccines and vaccine inputs and consequently the cost of vaccine administration and production. Of note in the discussion is the need to remove non-tariff measures, which do not serve any vaccine-specific purpose and instead delay the sourcing of vaccines and vaccine imports, thereby impeding access and raising costs. Equally important is increasing transparency in the administration of non-tariff measures, including through notifications to the World Trade Organization. The authors also highlight that non-tariff measures on vaccine-related inputs (e.g., syringes) could affect vaccination targets despite the availability of vaccines. Another important message is that countries must diversify their sources of imports for both vaccines and related inputs, given the potential vulnerabilities from overdependence on a few sources when there are supply chain disruptions and shocks. Trade policies should thus be designed with such diversification strategies in mind.

The discussion on trade-related policies and instruments also addresses the role regional and bilateral integration arrangements can play in improving equitable and affordable access to vaccines and essential health products. The authors point out that trade agreements can help not only by lowering restrictions on product imports, including of vaccines, but also by addressing health emergencies and building supply chain resilience through their provisions on standards, IP rights, trade facilitation, investment, government procurement, and mutual recognition, among others. In the context of trade liberalization, future trade agreements should aim for a comprehensive coverage of the health sector by including commitments to remove trade barriers, taking essential health products off exclusion lists, and avoiding inverted duties that disincentivize domestic manufacturing. With respect to non-tariff measures, countries are making efforts to align with international standards and to document, fast-track, and make transparent non-tariff regulations. The discussion notes the importance of complementing such national efforts with work on trade agreements to ensure time-bound commitments to conform to standards and processes, as well as regulatory cooperation for mutual recognition of standards and testing processes, and the use of templates for speedy clearance of medical
goods during pandemics and other health emergencies. The authors also stress that having simple and transparent rules of origin under trade agreements is important to enable value chain development for health products, as is including IP-related provisions that promote the transfer of technology for essential health products and sharing of data among partner countries. The discussion also highlights trade facilitation measures for essential health products, including fast-track procedures for emergency vaccines, complemented by regulatory cooperation measures for mutual recognition, as noted earlier. There is also scope for leveraging trade agreements through their provisions on investment, services, and mobility, among others, to address health sector accessibility and affordability considerations more broadly. Another important recommendation is to create mechanisms for sharing of best practices, exchange of information and data, and joint financing of R&D. The authors, however, stress that the measures taken under trade agreements need to be supported with appropriate domestic regulations and reforms, reconciling unilateral and cooperative action.

The discussion on value chains for vaccine production emphasizes fostering an efficient and effective ecosystem by focusing on two sets of policies. The first set involves increasing efficiency and scaling up existing capacity to handle demand surges during pandemics. The second set involves strengthening longer-term supply capacity by enabling the free flow of goods, building technical capacity, creating a conducive regulatory environment, encouraging public–private collaboration, and increasing value chain visibility to enable all players to make timely and effective decisions. The authors provide a decision tree outlining the necessary actions for pandemic preparedness across both these sets of policies. Firm-level considerations regarding innovation, marketing, pricing, and distribution strategies in shaping the vaccine value chain play an important role, thus giving rise to the significance of government policies in influencing these strategies. The discussion points out that starting up vaccine production or being part of the vaccine value chain should not be a goal for all countries as this depends on technological capacity. The focus thus should be first on achieving full and rapid vaccination of the population and then, depending on capacity considerations, determining the appropriate strategy for participating in the vaccine value chain, including collaboration with other governments and between private companies across countries.

The discussion on logistics highlights the many challenges affecting the cross-border delivery of vaccines. These include the lack of cold chain infrastructure in countries, problems with vaccine handling and transport due to inadequate skills and technology which lead to vaccine wastage and inefficacy, transport and regulatory bottlenecks, insufficient
funding, and the absence of trade facilitation measures such as fast-track procedures for emergency vaccines. Several policy recommendations are provided to address these constraints. The first is to harmonize policies and increase regulatory cooperation among countries to facilitate movement, clearance, and risk control. The second is to enhance regional cooperation to improve cold chain logistics planning and management. The third is to invest in building the skills and capacity of handling the customs procedures, including through knowledge sharing and cooperation among countries. The fourth recommendation is to establish mechanisms for cooperation and coordination among the various stakeholders involved in the vaccine distribution and delivery process, including customs and health authorities, importers, logistics service providers, and vaccine manufacturers, with the objective of increasing transparency, timely sharing of information, tracing, and expediting approvals while mitigating risks. Other policy recommendations include for individual countries to introduce measures to ramp up capacities of domestic logistics service providers and develop a national cold chain track and trace system.

Finally, this cluster of chapters explores the possibilities for cooperation among regulatory agencies across all segments of the vaccine cycle, from development, testing, approval, and manufacture to distribution. The discussion highlights the lessons learned from the recent pandemic, the gaps in policies and working procedures that need to be addressed to increase readiness among national regulatory authorities to face future health crises, and most importantly, the need to place cooperation between national regulatory authorities within the broader framework of longer-term international regulatory cooperation in medicines. With a view to supporting governments and public health authorities to improve the regulatory agility of national agencies in ensuring the quality, safety, and efficacy of medicines, one of the main recommendations is to maintain publicly available and up-to-date lists of approved medicines, using the WHO Model Lists of Essential Medicines for guidance, and to take the necessary steps to address related legislative, regulatory, and resource requirements for preparing such lists. Another recommended policy measure is to mandate time limits for national agencies to adopt and publish regulatory decisions. Prior to setting such time limits, it is recommended that governments review existing practices, previous cases of expedited decision-making from the pandemic which could be adopted permanently, and the necessary additional technical and financial resources, along with accountability measures to ensure adherence to these time limits. Countries that lack
the capacity or resources for medicines approvals are encouraged to use the WHO collaborative registration procedure for prequalified products upon completing a review of the cost–benefit implications of and factors constraining them from joining this process. The discussion also calls for cooperation between national regulatory authorities in different countries—either at the regional or multilateral level and ideally among agencies at similar maturity levels—and a dedicated capacity building program for national regulatory authorities with support from WHO and more established and well-capacitated National Regulatory Agencies (NRAs). Overall, there is scope for strengthening collaboration across different regulatory areas to exchange information, share experiences, and adopt effective measures to address public health concerns.

Overall, the recommendations across all the cross-border aspects of vaccine availability involve a mix of cooperative and collective efforts across countries, as well as measures within countries, thus underscoring the country-specific and global public goods dimensions of vaccine delivery.

12.2.3 National Distribution

The final set of chapters turns the discussion to the distribution of vaccines within countries. As the COVID-19 pandemic revealed, there was large variation in vaccine availability not only across countries but also within countries. Vaccine inequity is a challenge in many countries. Generally, vaccine coverage for disadvantaged, poor, and remote populations tends to be lower than for other groups. A major constraining factor is the lack of readiness of national health systems. Hence, health systems strengthening is the key. This will require accelerating universal health coverage by expanding primary care, increasing public funding, and prioritizing populations in fragile contexts. As undertaking such measures will come with challenges, governments—in partnership with the private sector—need to develop innovative financial and delivery mechanisms. This will also require reforms in the national health information system for delivering and managing health operations, such as establishing telehealth facilities, digital platforms, interoperable systems, and management of electronic health records, along with providing the requisite training of human resources and infrastructure development. Although the discussion focuses on the steps countries need to take nationally, cross-country learning and sharing of best practices and experiences remain relevant even in the case of domestic distribution of vaccines.
12.3 Final Thoughts and Future Work

This book has outlined a range of measures, both domestic and collective, cutting across the vaccine value chain from development to delivery, where steps need to be taken. Going forward, the analysis in this book raises several important questions to be addressed in future research if we are to create a framework that encompasses the recommended domestic and collective actions.

We focus here on a set of interrelated questions concerning the global health system. Specifically, how should the global health architecture be reformed to ensure affordable and equitable access to vaccines? To address this question, we need to examine the shortcomings of the current system, especially as highlighted by the pandemic. The proposed reforms should be able to better address the requirements of IP and technology transfer, trade, logistics, regulation, and national capacity that are critical for vaccine equity. In this context, what role can regional solutions or models play? How can regional approaches complement multilateral ones to achieve a more equitable response to ongoing and future infectious diseases threats? And which parts of the vaccine value chain are most conducive to a regional approach? This interest in exploring the role of regional models and solutions in ensuring vaccine coverage and health security is motivated by this book’s focus on Asia and the Pacific and the need to examine regional preparedness and the scope for regional cooperation in addressing future pandemics.

Several regional options are worth exploring in future work. While this book has highlighted some possible regional initiatives, we need to delve further to understand their mechanisms and approaches. For instance, regional technology transfer hubs could play a role in making vaccines less excludable and less rivalrous by enabling knowledge transfer and scaling local production. Further, regional pooled procurement involving countries with vaccine manufacturing capacity as well as importing countries could enable better terms of access and reduce risk and uncertainty. Another possible scheme is to have a regional technology platform, which holds promise for strengthening regional collaboration and addressing endemic diseases even in non-pandemic times. This platform could then provide a basis for adapting existing technologies and developing new ones during a pandemic. Likewise, regional financing mechanisms also require further examination. These initiatives could be along the lines of the Pan American Health Organization’s Revolving Fund for Access to Vaccines or the African Union’s African Vaccine Acquisition Trust, which could be emulated in Asia and the Pacific through subregional organizations such as the Association of Southeast Asian Nations. Regional trade agreements
provide another mechanism to keep trade flowing in times of crisis, enable harmonization of standards, and drive regulatory cooperation on trade facilitation, mutual recognition, traceability, technology transfer, and IP management, among others.

There are clearly many areas where having regional collective efforts and coordination alongside global and national efforts can be useful. Further research and analysis of existing examples and practices can help us to understand the strategic points in the vaccine value chain where such efforts would be most effective. Analyzing these issues would, however, raise its own set of difficult questions requiring further deliberation. For instance, how will the regional models coexist with global and national systems? What are the roles of different countries depending on their characteristics (producer and exporter, input provider, technology proprietor, pure importer, etc.) and the associated balance of power within the regional and global frameworks? What kind of interplay is needed between governments and the private sector within and across countries? A host of complex and dynamic issues would need to be addressed—with probably no concrete answers. As the discussion in this book has highlighted, however, the time is ripe to deliberate these difficult topics and to work at different levels simultaneously if we are to address the current shortcomings and prepare better for the future.
From Lab to Jab

Improving Asia and the Pacific’s Readiness to Produce and Deliver Vaccines

The coronavirus disease (COVID-19) pandemic highlighted the complexities and challenges associated with the development, production, and distribution of vaccines and the consequent risks and vulnerabilities arising from the lack of affordable and equitable access to essential vaccines and other health products.

This book identifies the challenges across the entire vaccine value chain from “lab to jab”—from research and development to the production and cross-border delivery of vaccines and their related inputs involving trade, transport, logistics and regulatory approvals, and finally to the distribution and administration of vaccines. These challenges include market failures, financing gaps, barriers to technology transfer, tariff and non-tariff barriers, transport and logistical constraints, lack of regulatory harmonization across countries, and limitations in the capacity of national health systems.

From Lab to Jab: Improving Asia and the Pacific’s Readiness to Produce and Deliver Vaccines underscores the need for unilateral and collective measures, such as coordinated efforts for financing, procurement, capacity building, needs assessments, and technology transfer. These can be implemented by leveraging trade and investment agreements, ensuring greater regulatory coordination, facilitating investments in national health systems, and sharing data, knowledge, and good practices across the region. The timely discussions call on vaccines to be viewed as a global public good. Hence, a combination of national, regional, and global mechanisms and platforms will be needed to ensure affordable and equitable access to vaccines in preparation for future pandemics.

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