



FROM LAB TO JAB · PRIORITY RESEARCH AREA 5

Regulatory Cooperation in Vaccines in the **Asia Pacific Region**

Improving Asia Pacific readiness to produce and deliver
vaccines

Contents

—	Abbreviations	3
—	Introduction	4
01	Framing the Discussion Vaccine cooperation as part of a broader regulatory dynamic	5
02	Regulation of Medicines History, processes and governance challenges	7
03	International Regulatory Cooperation in Medicines From networking to mutual recognition	10
04	Intergovernmental Cooperation and the COVID-19 Pandemic The race to develop and mass produce a vaccine	17
05	Regulatory Cooperation and Vaccines in Asia Pacific Reliance, regional financing and regional networks	20
06	Outlook and Policy Recommendations Five measures to improve regulatory agility	25
07	Concluding Remarks	31
REF	References and Further Reading	32
A-I	Future Preparedness Benchmarking Tool	38
A-II	Country Case Studies	42

The paper in numbers

8

regional economies examined at different stages of development and distances from the vaccine supply chain

India

China

Singapore

Cambodia

Viet Nam

Bangladesh

Vanuatu

Australia

5

forms of regulatory cooperation mapped, from informal networking to binding mutual recognition

5

policy recommendations to make national regulators faster and more resilient before the next pandemic

1

benchmarking tool for policymakers to assess regulatory and policy preparedness

Abbreviations

ADB	Asian Development Bank
ADRs	Adverse Drug Reactions
APVAX	Asia Pacific Vaccine Access Facility (ADB)
APEC	Asia Pacific Economic Cooperation
ASEAN	Association of South East Asian Nations
BLA	Biologics License Application (U.S. FDA)
CBER	Center for Biologics Evaluation and Research (U.S. FDA)
CDER	Center for Drug Evaluation and Research (U.S. FDA)
CHMP	Committee for Medicinal Products for Human Use (EU)
CPMP	Committee for Proprietary Medicinal Products (EU – superseded)
DCGI	Drugs Controller General of India
eCTD	Electronic Common Technical Document
EUL	Emergency Use Listing (WHO)
ESCAP	Economic and Social Commission for Asia and the Pacific (UN)
FDA	Food and Drug Administration (USA)
FD&C Act	Federal Food, Drug, and Cosmetic Act
EMA	European Medicines Agency
GCP	Good clinical practice
GLP	Good laboratory practice
GMP	Good manufacturing practice
GPvP	Good pharmacovigilance practice
ICMRA	International Coalition of Medicines Regulatory Authorities
IPC	Infection prevention and control

IND	Investigational New Drug (U.S. FDA)
JACG	Joint Assessment Coordination Group (ASEAN)
MedDRA	Medical Dictionary for Regulatory Activities
MHRA	Medicines and Healthcare products Regulatory Agency (UK)
HSA	Health Sciences Authority (Singapore)
NASEM	National Academies of Sciences, Engineering, and Medicine (U.S.)
NDA	New Drug Application (U.S. FDA)
NMPA	National Medical Products Administration of the State Council (China)
NRA	National drug regulatory authorities
PMS	Post-marketing surveillance
PPE	Personal protective equipment
PPWG	Pharmaceutical Products Working Group (ASEAN)
RAG	Regulatory Advisory Group (within COVAX)
SEARN	South-East Asia Regulatory Network (WHO)
SII	Serum Institute of India
SME	Small and Medium Sized Enterprise
SRA	Stringent Regulatory Authority
TGA	Therapeutic Goods Administration (Australia)
UN	United Nations
VTf	Vaccine Task Force (India)
WHO	World Health Organization
WTO	World Trade Organization

Introduction

The COVID-19 pandemic revealed many vulnerabilities in the economic, social and political fabric underpinning what much of the world had come to accept as normal.

The global health crisis that came to be known as the COVID-19 pandemic, and which started to sweep across the world in early 2020 shows no signs of abating at the time of writing (June 2022), due to the emergence of new variants and resulting fresh outbreaks in places that had previously been deemed to have vanquished the virus, such as the People's Republic of China. The pandemic revealed many vulnerabilities in the economic, social, and political fabric underpinning what much of the world had come to accept as normal. In ways that we are still grappling to understand (since the dust has not yet completely settled), the pandemic and the many disruptions it brought about, have ushered in significant changes to the way we work, consume, spend our leisure time, and even our relationships to government. In many ways, the pandemic has wrought a significant realignment between citizens and governments, both in terms of the expectations the former have of the latter and the powers the latter claims and exerts over the former (Brown, Brechenmacher and Carothers, 2020).

After first framing the discussion and delimiting the paper's scope in **Section 1**, this contribution then turns its focus to a general discussion of the ways in which medicines (of which vaccines are a subset) are regulated today and what goals governments generally pursue in this policy area - **Section 2**. Next the paper turns to an examination of international regulatory cooperation in medicines - **Section 3**. **Section 4** then discusses the unprecedented levels of international cooperation seen in response to the COVID-19 pandemic between not only governments but also the private sector and non-governmental organizations, before **Section 5** then turns to an examination of reg-

ulatory cooperation in the area of vaccines in the Asia Pacific. Finally, **Section 6** discusses the present outlook while also setting out some policy recommendations for governments going forward.

Throughout our research, although we took into consideration efforts and initiatives at the global level, we focused our attention on the experiences of governments and other actors in and as they relate to the **following regional economies**:

1. India
2. People's Republic of China
3. Singapore
4. Cambodia
5. Vietnam
6. Bangladesh
7. Vanuatu
8. Australia

This selection was made because it represents a fair sample of different-sized regional economies at varying degrees of economic development and at various removes from the global vaccine supply chain (discussed in another contribution to this series).

Throughout the paper, we present a number of case studies on how each of these economies dealt with the pandemic, its economic impact and the race to produce or procure and then rollout vaccines.

An annex to this report contains a Future Preparedness Regulatory and Policy Benchmarking Tool to guide policymakers and political leaders in future efforts at improving the regulatory structures and processes discussed in this paper.

Framing the Discussion

IN THIS SECTION

1.1 International Regulatory Cooperation in Vaccines Part of a Broader Dynamic

1.2 International Regulatory Cooperation in Other Related Products

1.3 Scope Limitations of the Current Research

1.4 COVID-19 Pandemic a Time for Moving Fast and Breaking Things

Vaccine cooperation as part of a broader regulatory dynamic, and the scope of this research.

This paper explores the massive strides that were made in response to the COVID-19 pandemic by national drug regulatory agencies (NRAs) in order to achieve what ultimately became the fastest instance in human history of the development, testing, approval, manufacture, and distribution of a new vaccine to an infectious respiratory disease that at the time of writing has by some estimates claimed over 6 million human lives.¹ Our purpose in writing this paper is to highlight what regulators did right, where the pandemic shone a light on gaps, and what can be done by national governments to increase readiness in their NRAs for the next time they are called upon to execute their role in a similar herculean effort.

1.1 International Regulatory Cooperation in Vaccines Part of a Broader Dynamic

International regulatory cooperation in vaccines is but a small part of international regulatory cooperation in the area of medicines. However, its importance has been thrust to center stage recently as a result of the COVID-19 pandemic with governments all over the world moving at breakneck speed to inoculate their populations with a completely new generation of vaccines, in some cases based on revolutionary new technologies.² Because it is embedded in the broader processes of international cooperation between national authorities tasked with the approval of new medicines, namely NRAs, our discussion of this

subject is likewise inevitably framed within the wider structures that characterize international regulatory cooperation in medicines, of which vaccines are but a subset.³

1.2 International Regulatory Cooperation in Other Related Products

The scope of international regulatory harmonization and cooperation goes beyond medicines and vaccines and covers a broad array of related products, including personal protective equipment (PPE), medical devices (such as ventilators), in-vitro diagnostic tools, and even hand sanitizer. All of these products became centrally important during the COVID-19 pandemic, and as will be discussed in Sections 4 and 5 below, the pandemic saw rapid changes to existing structures and procedures that saw NRAs embrace the (hitherto almost unknown or at least largely unarticulated) concepts of regulatory flexibility or agility (European Commission 2020). We discuss some of these actions in more detail below, **however, our focus remains predominantly on vaccines.**

1.3 Scope Limitations of the Current Research

The world has changed a lot due to the COVID-19 pandemic, and there are many ways in which public health systems and peoples' expectations of them

have been forever and profoundly transformed. This is likewise true of regulatory harmonization and cooperation between NRAs, where the urgency that the pandemic and its economic and social aftermath gave rise to, required regulators across a broad range of fields and areas of government activity to find new ways of doing things, many of which were simply not possible without working with their counterparts in other countries. In this contribution, given the time and space constraints, we have chosen to focus primarily on international regulatory cooperation in the area of vaccines.

1.4 COVID-19 Pandemic a Time for Moving Fast and Breaking Things

As discussed in more detail in Sections 4 and 5 of this paper, the sheer scale of COVID-19 and the urgency felt by political leaders everywhere to gain control over the virus and navigate a return to socio-economic normality precipitated rapid and coordinated action to develop, test, authorize, mass-produce and distribute a vaccine on a hitherto unprecedented scale and at likewise unprecedented speed. There were many moving parts and different stakeholders in these various processes, all driving towards the same goal of in-

oculating as much of mankind against the virus as soon as possible.

One aspect of this urgent collaboration, which is the focus of this paper, was a hitherto unprecedented degree of cooperation between NRAs to authorize the use of as many new vaccines as possible, leading to what some observers have termed regulatory agility (Lim 2020, Bolislis et al 2021). This agility manifested itself in various forms, including expedited reviews and approvals, innovative approaches to streamline clinical trials, offering to conduct inspections of production facilities on a remote or virtual basis, flexible approaches to labelling, adoption of digital and online technologies to facilitate communication and interaction between regulators and other stakeholders (Bolislis et al 2021).

This paper concludes with a number of policy recommendations that seek to entrench the many gains and much of the forward momentum achieved during the pandemic on regulatory harmonization, so that the many lessons learned are not lost and so that the state of preparedness for future public health crises does not regress to pre COVID-19 levels, where they were obviously found wanting in many countries.

NOTES

1 This figure from Our World in Data, last updated per the end of April 2022.

2 This was the case with a number of vaccines based on so-called mRNA technologies. See, among many, Dolgin 2021.

3 The Australian Therapeutic Goods Administration (TGA) describes vaccines as “medicines that protect you against specific diseases” (<https://www.tga.gov.au/vaccines-overview>) whereas the US Food and Drug Administration (FDA) offers several definitions of what comprises a drug, including “a substance intended for use in the diagnosis, cure, mitigation, treatment, or **prevention** of disease (emphasis added – <https://www.fda.gov/drugs/drug-approvals-and-databases/drugs-fda-glossary-terms>). The European Medicines Agency (EMA) for its part, defines a medicinal product as “a substance or combination of substances that is intended to treat, **prevent** or diagnose a disease” (emphasis added – <https://www.ema.europa.eu/en/glossary/medicinal-product>).

Regulation of Medicines

IN THIS SECTION

2.1 Different Aspects of Modern-Day Regulation

2.2 Historical Pedigree

2.3 Progress Through Crisis Response

2.4 Processes and Procedures

2.5 Technical Complexity and Governance Challenges

How medicines are regulated today, where that practice came from, and the governance challenges regulators face.

This section seeks to place the regulation of vaccines in its substantive context, namely within the broader framework of how medicines (of which vaccines are an important subcategory) are regulated. In doing so, it first discusses different aspects of how medicines are regulated in the modern economy, before turning to a discussion of the historical pedigree of medical regulation. It then discusses how various public health crises have historically proven to be such important catalysts not only for new medical breakthroughs but also for regulation of the sector more generally and for increasing the responsiveness of regulators to public demands in particular. Next, this section discusses a number of processes and procedures that are at the heart of modern regulation of this sector before concluding with a discussion of both the technical complexity and governance challenges that pervade modern regulatory systems.

2.1 Different Aspects of Modern-Day Regulation

The distribution and consumption of medicines is regulated to one degree or another in almost all countries today. Regulation typically covers a number of areas, including but not limited to: 1) evaluation of data on the safety and efficacy of new drugs over the course of various trial stages (animal or human); 2) inspection and certification (licensing) of manufacturing facilities and distribution channels against contamination risks; 3) pre- or post-marketing monitor-

ing of any reported adverse drug reactions (ADRs); and 4) ensuring that safety and efficacy claims made in relation to approved medicines in promotional and advertising materials are accurate (Britannica, 2021).⁴ International regulatory cooperation (as discussed in more detail in subsequent sections of this paper), happens to varying degrees across all of these areas of activity but is arguably the most widespread in terms of (1) and (2). For these reasons, the lion's share of the analysis offered here likewise relates to these two regulatory functions and where international cooperation focuses on strengthening and improving them.

2.2 Historical Pedigree

The approval of vaccines for public use, like the pre-market approval of medicines more generally, has a long historical pedigree going back to the manufacture of Mithridatum and Theriac (Griffin 2004), and today follows well-defined (albeit not harmonized) procedures in many countries. Comparative studies have shown that despite efforts over the last 30 years at regulatory harmonization, starting in Europe but also in other regions such as South East Asia, East Africa and the Americas (Regi 2017; Ndomondo-Sigonda et al 2021; and PAHO 2019), a high degree of variance remains between countries with regard to the form these procedures take, their duration, complexity, cost and the regulatory burden they impose more generally (Dukes 1986, Pezzola and Sweet 2016), not to mention the downstream impacts these varia-

tions exert on industry structures (Daemmrich 2009) and (more importantly) peoples' access to medicines (Roth et al 2018). These variations exist and persist despite the vast majority of these agencies essentially sharing the same fundamental goal, i.e., ensuring that new drugs are safe, efficacious and of high quality (NASEM 2020).

2.3 Progress Through Crisis Response

The process of establishing and improving the regulation of medicines, particularly in advanced industrialized countries, has often been in response to a related health crisis. For example, Ballentine (1981), as well as Thind and Kowey (2021), discuss the 1937 Elixir Sulfanilamide Incident, 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 (FD&C Act).⁵

By the same token, Abed (2014) discusses the role the thalidomide tragedy of the 1960s played in the formation of new regulatory agencies throughout Europe. On a related note, Daemmrich (2009) goes into some detail on the impact that the AIDS crisis had on the U.S. FDA, particularly with respect to expedited approval of new and experimental medicines and treatments, and notes that a similar effect was largely absent from the European regulatory scene. As we will show later, the current (at the time of writing) COVID-19 pandemic has had a similarly dramatic impact on several important aspects of both the regulatory approval process at the national level as well as international regulatory cooperation in vaccines.

2.4 Processes and Procedures

The procedural modalities linked to gaining approval for a new drug differ from country to country, although there are a number of commonalities.⁶ One of the most important and resource intensive steps, and in fact the first step that is specifically characterized by the involvement of the regulator, is the submission of an application by the sponsoring drug maker to investigate a new potential drug. In the U.S., this is called an Investigational New Drug (IND) application (Holbein, 2009, FDA 2021). In the EU, the national regulatory authorities in the different Member States are responsible for approving and overseeing clinical

trials conducted on their own respective populations, albeit subject to standards and procedures adopted under EU law (EMA, 2019).

The IND application with the FDA's Center for Drug Evaluation and Research (CDER) seeks approval to proceed with human clinical trials and will generally consist of information the drug maker has compiled (in pre-clinical testing) on three essential test criteria, namely: 1) toxicity and pharmacology of the drug demonstrate that the drugs can be safely administered to human test subjects; 2) the ability to safely and consistently manufacture large batches of the drug to the same levels of quality; and 3) 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 test criteria represent a high barrier for drug makers to clear before their products are approved to enter the market. Lesko and Woodcock (2004) posit that over 80 percent 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 take place in three phases. Phase I involves small numbers (between 20 and 80) of healthy volunteers, with the main objective of this phase being 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 of which are afflicted with the underlying pathological condition the drug is intended to treat. Here the emphasis is on determining the drug's efficacy and in particular on determining a so-called therapeutic dosage window, meaning a dose at which "the efficacy and side effects are optimally balanced" (Thind and Kowey, 2021). 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).

Only after Phase III trials have been successfully concluded does the sponsoring drug maker submit a New Drug Application (NDA) again to the FDA's CDER.⁷ 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 find-

ings resulting from the entirety of pre-clinical and clinical trials, information that will be provided to consumers on the drug's labelling, and the facilities where the drug is manufactured (FDA, 2015). It should be noted, however, that vaccines, being biological products, follow a parallel pathway in the U.S.: although they too begin with an IND application, they are reviewed not by CDER but by the FDA's Center for Biologics Evaluation and Research (CBER), and are licensed on the basis of a Biologics License Application (BLA) under the Public Health Service Act rather than an NDA. The procedural logic described above nonetheless applies to both.

2.5 Technical Complexity and Governance Challenges

Even a cursory browse through the available literature on the approval procedures for new medicines is enough to drive home the inherent technical complexity of this task. This complexity comes in various forms, both in terms of the scientific and clinical knowledge required, but also the underlying governance structures that should ideally be in place in order to ensure that conflicts of interest and external pressures can be properly managed. Indeed, managing these governance challenges and mastering the scientific and clinical knowledge required are essential if the regulator is to meaningfully pursue and perform its core public health objective, namely, to ensure that drugs are safe, efficacious and of high quality. Even in advanced industrialized countries, regulators find this

challenging (Hawthorne, 2005 and Carpenter 2010). Clearly there is an important development dimension here given that many developing countries will lack either or both of these preconditions (Pezzola and Sweet, 2016).⁸

Yet another aspect that is important from a development perspective is that other factors beyond the above-mentioned asymmetries in expertise and governance also play an important role in constraining access to medicines for people in developing countries. The most important of these other factors is arguably that most of the largest as well as the most innovative drug makers are from advanced industrialized countries and prefer seeking marketing approval in either their home markets or other similarly endowed countries with regulatory structures and processes that they are already familiar with. The second other factor that favours the development and marketing of new drugs in advanced industrialized countries before they become available in the developing world is the fact that the former represent the most lucrative markets for generating returns for these drugs, simply because of the purchasing power of their resident populations and/or the fact that most residents enjoy some form of health insurance that covers the cost of these drugs (WHO, 2017). We discuss further development-related implications in subsequent sections of this paper, particularly when addressing the uneven distribution we have seen with regard to COVID-19 vaccines and the vastly different outcomes this has produced in developed and developing countries worldwide.

NOTES

⁴ Wang and Wertheimer (2021) add a number of other activities to this list, including development of regulatory policy and guidance, surveillance priorities and inspection programs, enforcement action clearance responsibility, and testing research.

⁵ 21 U.S.C. ch. 9 §301 et seq.

⁶ Here we base our discussions primarily on the processes and procedures (and terminology) established and followed by the U.S. FDA.

⁷ In the EU, the corresponding procedure is called a market authorisation application, see EMA, (2019).

⁸ The WHO in fact distinguished between four categories or "maturity levels" in terms of the technical and regulatory capacities of NRAs and the governance systems within which they operate, with level 1 being the least mature and levels 3 and 4 being the most mature. Using its Global Benchmarking Tool (GBT), the WHO has determined that with respect to the current status of regulatory systems for medicines and vaccines, some 100 countries are at Maturity Level 1, meaning only some elements of a regulatory system exist, with another 44 countries at Maturity Level 2 meaning that an evolving regulatory system is present that partially performs essential regulatory functions. The WHO furthermore notes that 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 (see WHO 2021b).

International Regulatory Cooperation in Medicines

IN THIS SECTION

3.1 A Brief History

3.2 Factors Driving Regulatory Cooperation

3.3 Forms of Regulatory Cooperation

3.4 Multilateral-Driven Cooperation by WHO

3.5 International Coalition of Medicines Regulatory Authorities (ICMRA)

3.6 Regional Cooperation Mechanisms

National regulatory authorities cooperate in forms ranging from informal networking to binding agreements, along a gradient of steadily increasing formality and trust.

This section discusses the evolution of regulatory cooperation between different NRAs and how this process functioned pre the COVID-19 pandemic (which is discussed in Section 4 of this paper). In doing so, it focuses first on the European experience, since this is where international regulatory cooperation between different NRAs was first successfully pioneered. It then turns to the factors that drive regulatory cooperation and the forms this takes today. Next, this section discusses a number of multilateral and regional approaches to regulatory cooperation, whereby a more in-depth appraisal of this phenomenon in the APAC region is the focus in Section 5 of this paper.

3.1 A Brief History

3.1.1 The European Experience

The forerunner of what we now understand as international regulatory cooperation in medicines can be found in the process of gradual harmonization that took place over the course of several decades of European integration. The initial foray into aligning different regulatory approaches was taken in 1965 with Council Directive 65/65/EEC.⁹ This Directive sought to approximate procedures and standards in a number of important ways, including the principle that no medicine shall be placed on the market without prior approval (Art. 3), a set of minimum formal and substantive requirements for drug makers to meet before such approval can be granted (Art. 4), time-limits within which national regulators must review

and decide upon applications for market approval from drug makers (120 days, with an additional 90 days possible under exceptional circumstances - Art. 7), the period for which such approvals are to be valid (5 years - Art. 10), enforcement actions related to post-market surveillance (Art. 11), and due process provisions incumbent upon Member-State NRAs with respect to their decision-making powers under the Directive (Art. 12). The 1965 Directive also sets out minimum requirements with regard to drug labelling (Art. 13 - 19). Interestingly for those who follow the various controversies over tensions between public health and trade liberalization, the 5th and 6th recitals of Directive 65/65/EEC appear, at first glance, to tilt this question in favor of the latter. Whereas the 5th Recital firmly acknowledges the primary purpose of rules on the production and distribution of medicines is to safeguard public health, this is immediately caveated by the 6th Recital which states

Whereas, however, this objective must be attained by means which will not hinder the development of the pharmaceutical industry or trade in medicinal products within the Community.

This may seem surprising to a modern observer (although the recital is perhaps best read as an early expression of the proportionality principle that runs through single-market law, rather than as a ranking of trade above health), since today - at least rhetorically

- primacy is afforded to public health as a so-called higher-order priority, whereas the needs of industry and the imperatives of trade liberalization are often relegated to the status of subordinate interests. This likewise corresponds to the language of the GATT and GATS general exceptions, which – under certain conditions – afford governments the ability to set aside their WTO obligations if this is done in order to protect public health (WHO and WTO Secretariat 2004).

The process of regulatory harmonization took another big step forward in 1975, with the adoption of two new Council Directives; one on clinical testing of medicines prior to their marketing approval (Council Directive 75/318/EEC)¹⁰ 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).¹¹ The 1975 Directives also provided for the establishment of the first supranational body in the regulation of medicines in the EU, namely the Committee for Proprietary Medicinal Products (CPMP), intended to “help EU Member States to adopt a common position with regard to decisions on issuing a marketing authorisation” (Abed 2014). The activities of the CPMP, discussed at some length by Sauer (2019) in his retelling of regulatory harmonization in Europe and beyond, provided a firm basis for national regulators and experts to work together and build the trust so essential to deeper and more formalized expressions of regulatory cooperation (Golberg 2020). More importantly, the development, by experts from governments, industry, and academia across Europe, of detailed technical guidelines covering many aspects of the approval process including quality, safety, and efficacy testing, as well as good manufacturing practices, set the stage for broader international cooperation and harmonization. As Sauer (2019), himself intimately involved with this process since the 1970s and the first Executive Director of the European Medicines Agency after it was established in 1995, notes

The availability of pharmaceutical legislation in all EU official languages had a deep impact on many continents. Scientists from all parts of the world had an [sic!] easy access to a consistent body of scientific guidelines and procedural advice to applicant [sic!] (in English).

Today, the EU still operates according to a model that sees national regulatory bodies working with the European Medicines Agency on the basis of standards and procedures harmonized at the EU level, with the national agencies taking the lead in overseeing early clinical trials of new medicines – a role managed by the FDA in the U.S., with the latter working together with a local institutional review board (IRB).¹² The Member-State NRAs in the EU also play an important role in performing post-marketing surveillance (PMS) (Gough, 2005). The EMA plays a key role in what is today known as the centralized procedure. The institutional successor to the aforementioned CPMP is today the Committee for Medicinal Products for Human Use (CHMP) of the EMA, which is the equivalent to the FDA’s CDER (discussed above). It is the CHMP which conducts the scientific evaluation of a marketing authorization application, and which issues its opinion on whether or not to approve a drug for marketing to the general public. This opinion is then forwarded to the European Commission, which issues a legally binding decision on the marketing authorization, that is valid not only for the 27 countries of the EU, but also Iceland, Liechtenstein, and Norway (although importantly not Switzerland, which as the home country of some of the world’s largest pharmaceutical companies, has its own stringent regulatory authority, Swissmedic).

3.1.2 First Steps at International Regulatory Cooperation

1990 saw the launch of the International Conference for the Harmonisation of Pharmaceutical Requirements (ICH) between the EU, USA and Japan, with the goal being to “reduce unnecessary repetition of tests in humans and animals and duplication of costly stability and quality controls ... without compromising public health” (Sauer 2019). This initiative was launched at the behest of the European Commission and brought together actors comprising both government regulators and associations representing the research-based pharmaceutical industries in these regions (Lindström-Gommers and Mullin 2019). Over time, participation in biannual ICH meetings would grow to include experts and regulators from the, WHO, Canada, Switzerland and the global industry body, the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), which also provided the Conference with a secretariat. This

mostly informal system of regular meetings and ongoing working groups was superseded by regional events and – in 2015 – the establishment of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (which retained the same acronym – 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 significant outcomes including a dizzying array of guidelines under four distinctly classified areas, namely quality, safety, efficacy and multidisciplinary (i.e., cross-cutting). As the ICH itself notes, some of the harmonization outcomes achieved in the category of quality, include “defining relevant thresholds for impurities testing and a more flexible approach to pharmaceutical quality based on Good Manufacturing Practice (GMP) risk management”. By the same token, the ICH touts some of its achievements in the area of safety, including “a comprehensive set of safety Guidelines to uncover potential risks like carcinogenicity, genotoxicity and reprotoxicity” (ICH, 2021). A landmark set of outcomes, work on which began in the earliest days of cooperation, and which have culminated in widely accepted norms, include a common electronic format for applications – the Electronic Common Technical Document (eCTD) – and a common terminology – the Medical Dictionary for Regulatory Activities (MedDRA) (Sauer 2019, Lindström-Gommers and Mullin 2019).

3.2 Factors Driving Regulatory Cooperation

3.2.1 Asymmetries in Resources and Capabilities Between NRAs

As discussed above, the regulatory cooperation and ultimately harmonization that took place in the context of European integration was driven by the overarching imperative of creating a single market for the free circulation of all goods in Europe, including medicines. Today, a number of other imperatives are driving regulatory cooperation. One of these, also briefly alluded to above is the recognition that effective drug regulation is both complex and highly resource intensive. Only a handful of NRAs in the world arguably are capable of effectively managing 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 struggle to fulfill their mandates to the complete satisfaction of all relevant stakeholders (drug companies, the public, doctors, patient advocacy groups, public-health NGOs, political leaders and others). Even the WHO recognizes this, and attributes this to “globalization of markets, the sophistication of health technologies, the rapid evolution of regulatory science and the increasing complexity of supply chains”, all of which conspire to make it unavoidable that NRAs “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 at p. 240).

3.2.2 Growing Complexity of Supply Chains

In their 2020 consensus study report on global trends in regulating medicine, NASEM come to the same conclusion, noting that “[drug] development, authorization, and regulatory supervision have become international endeavors, with most medicines now being global commodities” (preface). The report goes on to specify that “China is now the leading producer and exporter of APIs by volume, manufacturing more than 2,000 APIs” (p. 72), while India has also become a major production center, as its pharmaceutical sector “accounts for 71 percent of the market share of generic drugs and supplies more than 50 percent of the world’s vaccines” (p. 73). The committee which authored the report concludes that “protecting and promoting public health in a time of globalization and unprecedented advances in technology and medicines—which are mirrored by the 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).

3.3 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 (see footnote 8), the WHO describes the objectives of its Regulatory

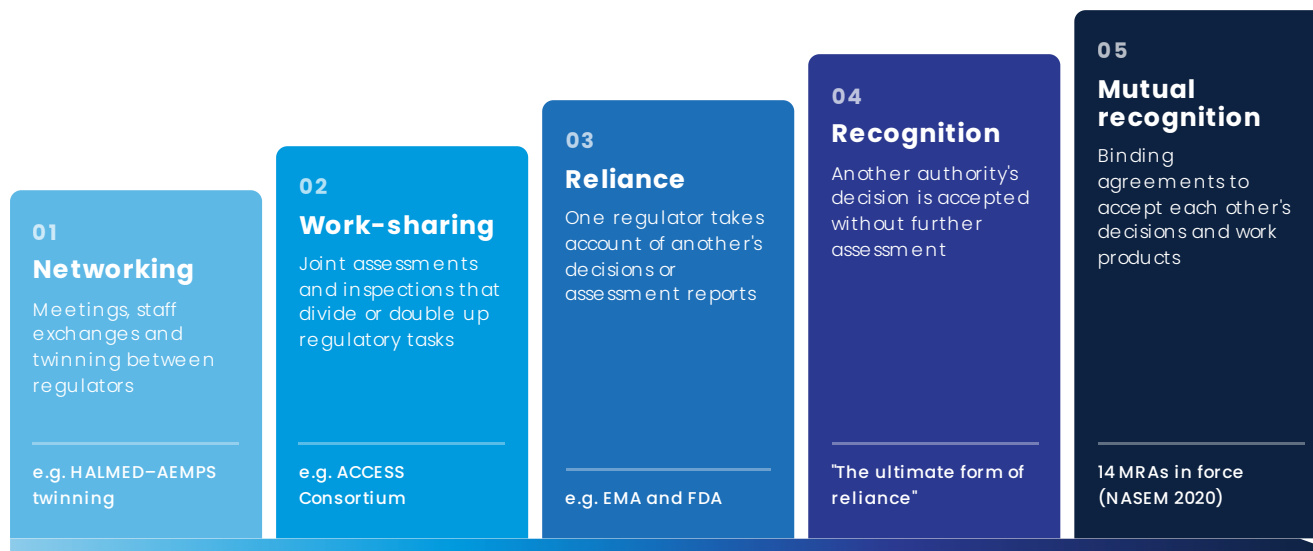
System Strengthening program, and in doing so defines one of these objectives as to promote regulatory cooperation, convergence and transparency through three activities, namely 1) networking, 2) work-sharing, and 3) reliance (Khadem 2019).¹³ This section ex-

plores these three forms of regulatory cooperation in more detail, together with two more formalized variants of reliance, namely recognition and mutual recognition.

LOWER FORMALITY

FIGURE 3.1 · FORMS OF REGULATORY COOPERATION

HIGHER TRUST



Source: Authors, based on WHO (2021b), Khadem Broojerdi et al. (2020) and NASEM (2020).

3.3.1 Networking

Networking between NRAs has already been taking place for several decades thanks to the regular meetings organized under the auspices of the International Conference for the Harmonisation of Pharmaceutical Requirements. As already mentioned, this began first between regulators from the U.S., EU, and Japan, before expanding 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 above).

Various other fora exist that allow regulators from different NRAs to meet informally albeit to discuss and share expertise on substantive areas of expertise, the most important of which is of course the WHO itself, which organizes dozens of meetings every year, both in Geneva but also at the regional level. Other multi-lateral and regional organizations do the same, such as the WTO, the UN, the World Bank, the Asian Development Bank, APEC, ASEAN etc. (regional cooperation efforts are discussed in more detail in Section 3.6 below).

Networking activities between regulatory agencies might also include twinning of regulatory agencies, staff visits and exchanges (Ndomondo-Sigonda et al 2017; WHO 2021b). For example, the Croatian NRA HALMED¹⁴, as part of its extensive and multi-year capacity building efforts in the context of the country's accession to the European Union, undertook a twinning program with its Spanish counterpart AEMPS.¹⁵ This program lasted from December 2010 to June 2011 and involved 11 visits by 30 AEMPS officials to conduct training seminars and workshops, as well as 2 study tours by HALMED staff to the Spanish official medical control laboratory (OMCL) network partner - see immediately below - (Tomić 2011).

3.3.2 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" and goes on to note that "[t]he opportunities for work-sharing include joint assessment of applications for authorization of clinical trials or marketing authorizations, 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). Work-sharing is thus an important mechanism for building the trust that is so essential if NRAs are to be able to practice reliance (discussed immediately below) to any meaningful degree (NASEM 2020). One example of such a work-sharing arrangement is that of the Australia–Canada–Singapore–Switzerland–United Kingdom (ACCESS) Consortium, formed in 2007, and which sees NRAs from these countries working together on initiatives such as the New Active Substance Work-Sharing Initiative (NASWSI) (TGA 2021a). The Consortium describes its goal as “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 2021b).

A distinct form of work-sharing is a joint activity, joint assessment or joint 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”. The 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 in order to share their assessments, benefit from each other’s expertise and discuss any shortcomings of the data evaluated” (WHO 2021b). In the case of a joint assessment, this may involve an application being submitted to two separate NRAs concurrently, allowing them to conduct their evaluations at the same time and share any findings and conclusions they reach. This also reduces the possibility that an important factor may be overlooked or underappreciated. A joint inspection by the same token would involve staff from two separate NRAs conducting an inspection of the same facilities, (either simultaneously or asynchronously), with each authority being tasked with different and discrete aspects and elements of the inspection in question (WHO 2021b).

3.3.3 Reliance

The most important instance of regulatory cooperation is reliance, which can manifest itself in various ways along a gradient of steadily increasing formality. The report by NASEM cited above refers to the range of different approaches and methods to facilitate reliance (and recognition discussed below) as “arrangements” and acknowledges that these can be more or less formalized in their conceptualization and opera-

tion. For example, the establishment of ad hoc committees, working parties or other dedicated working groups assembled to focus on a specific API or set of processes constitute less formalized expressions of reliance, whereas memoranda of understanding (MoUs), confidentiality agreements or mutual recognition agreements (MRAs) – the latter of which are particularly important in the area of medicines – are all more formalized instruments by means of which regulatory cooperation takes place and through which NRAs share the considerable burdens that NRAs must bear.

Reliance can also be categorized as either horizontal or unidirectional.¹⁶ The former takes place between NRAs that operate at roughly the same level of technical sophistication and resource-endowment, such as between those discussed above in the context of the ACCESS Consortium, or between the EMA and the FDA. Unidirectional reliance on the other hand 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.

3.3.4 Recognition

Recognition is a subgroup of reliance and has been termed “the ultimate form of reliance” (NASEM 2020). The WHO categorizes this form of cooperation as “a special and more formalized approach to reliance” and goes on to articulate that this involves one NRA recognizing “the decisions of another regulatory authority, system or institution, obviating additional regulatory assessment to reach its own decision”. (WHO 2021b, p. 245). NASEM, in its 2020 report, notes that the unwillingness of some NRAs to share completely unredacted decisions or assessment reports represents a serious constraint on the ability of dependent NRAs to rely on these works, and accordingly NASEM advocates for the sharing of unredacted documents (NASEM 2020, p 13).

3.3.5 Mutual Recognition

Mutual recognition has taken on overarching importance in the area of regulatory cooperation between NRAs and is a formal instrument by means of which two NRAs agree to recognize each other’s decisions and/or work products. Mutual recognition is usually predicated on binding agreements either between

the cooperating NRAs, or they take the form of binding international treaties negotiated at the level of governments. (WHO 2021b). The 2020 NASEM report lists 14 MRAs currently in force in the area of regulation of medicines, all of which are between NRAs that can be considered the “most mature” under the WHO nomenclature (Khadem Broojerdi et al 2020).¹⁷ These MRAs typically concern issues or processes such as GMP inspections, batch certification, product, packaging and labelling standards, conformity assessment requirements, GLP inspections and acceptance of industrial products (NASEM 2020).

There are a number of proposals to increase the impact of mutual recognition, including decoupling them from trade agreements (where they are usually negotiated) so that they may be bilaterally worked out between NRAs directly. This, it is argued, would allow these agreements to be concluded faster and without being held hostage to the other (unrelated) bargaining and concessions which typically characterise the horse-trading that makes the negotiations of trade agreements such a protracted matter. Another recommendation is to expand their substantive scope beyond the limited set of issues they currently cover (see immediately above).

3.4 Multilateral-Driven Cooperation by WHO

It is hard to overstate the importance of the WHO in terms of its contribution to regulatory cooperation between NRAs. This contribution has already discussed the WHO's efforts in Regulatory System Strengthening (RSS) through its Benchmarking Tool (WHO 2021b). Other ways in which the WHO supports regulatory strengthening and harmonization activities is by developing common standards for pharmaceutical processes and regulation, as well as supporting the regional cooperation mechanisms discussed immediately above. The WHO's Prequalification Program can result in accelerated marketing authorizations for medicines in as little as three months (ADB 2016). As discussed in Section 4 below, the WHO likewise took on a central role in the international regulatory cooperation that characterized the race to vaccinate humanity against the 2019 novel coronavirus.

3.5 International Coalition of Medicines Regulatory Authorities (ICMRA)

The ICMRA was established in 2012 in the face of growing recognition by the heads of a number of 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). A number of the specific challenges this initiative seeks to address include the growing complexity in both “manufacturing and distribution supply chains for medicinal products” and in “medicinal products and their ingredients (e.g. new chemical entities and innovative drugs)” (ICMRA 2021). At the time of writing (June 2022), the ICMRA comprises some 24 member NRAs from countries as diverse as Australia, the EU, USA, Japan, South Korea, Mexico, India, Nigeria, South Africa and China (ICMRA 2021). In addition to its member NRAs, the ICMRA also has associate members from 13 countries at different maturity levels, and the WHO as a permanent observer. As discussed in Section 4 below, the ICMRA assumed a key function in the race to approve and distribute vaccines at the height of the COVID-19 pandemic.

3.6 Regional Cooperation Mechanisms

A number of regional initiatives have proven highly effective at promoting cooperation of one of the forms discussed in the previous section, and this is true across regions as diverse as East Africa, Southern Africa, the Americas, and the Asia Pacific. To name just one example from Sub-Saharan Africa, the so-called ZAZIBONA process (involving NRAs from Zambia, Zimbabwe, Botswana and Namibia), which is a collaborative procedure for registration of medicines under the auspices of the Southern African Development Community (SADC), managed to shorten timelines for drug registration 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), as well as developing regulatory reliance principles that informed the WHO’s subsequent work on good reliance practices (PAHO 2019).

In the Asia-Pacific region, a number of initiatives stand out, including the Pharmaceutical Products Working Group of ASEAN, which “has developed its own guidelines on technical requirements and what information marketing authorization applications

should include” (ADB 2016). Another highly relevant initiative in the region is the Asia-Pacific Economic Cooperation (APEC) Life Sciences Innovation Forum, which convenes a Regulatory Harmonization Steering Committee whose aim is to “promote a coordinated approach to medical product regulatory harmonization and capacity-building efforts within the APEC region” (ADB 2016). This paper discusses regulatory cooperation in the APAC region in more detail in Section 5.

NOTES

9 Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by Law, Regulation or Administrative Action relating to proprietary medicinal products (Official Journal 022, 09/02/1965 P. 0369 – 0373).

10 Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of Member States relating to analytical, pharmacotoxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products (OJ L 147, 9.6.1975, p. 1–12).

11 Second Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by Law, Regulation or Administrative Action relating to proprietary medicinal products (OJ L 147, 9.6.1975, p. 13–22).

12 An IRB is described by the FDA as an “appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects” (FDA, 2018).

13 The other objective of this program, in fact the first, is – as the name *Regulatory System Strengthening* suggests – to “build regulatory capacity in Member States consistent with good regulatory practices”.

14 HALMED stands for Agency for Medicinal Products and Medical Devices of Croatia.

15 AEMPS stands for Spanish Agency for Medicine and Health Products.

16 These terms are borrowed from the 2020 report of the U.S. National Academies of Sciences, Engineering and Medicine cited above.

17 The 14 MRAs in question are all between NRAs in either Australia, Canada, the European Union, Israel, Japan, Iceland, Liechtenstein, New Zealand, Norway and the United States.

Intergovernmental Cooperation and the COVID-19 Pandemic

IN THIS SECTION

4.1 Initial Responses from the G20

4.2 Multilateral Responses from Diverse Sectors

4.3 The Race to Develop and Mass Produce a Vaccine

4.4 Making a Virtue out of Necessity through Regulatory Agility

Unprecedented cooperation between governments, the private sector and non-governmental organisations in the race to develop and mass produce a vaccine.

4.1 Initial Responses from the G20

The pandemic saw a scramble among countries to acquire scarce resources in the initial demand and supply shocks that characterized the first weeks and months of the COVID-19 crisis (Tooze 2021, Bradley 2020; OECD 2020). This period was primarily one of competition and not cooperation, but this quickly changed. By the end of March 2020, barely two weeks after the WHO had declared the outbreak a pandemic, G20 leaders convened an extraordinary summit and had pledged a series of actions, including 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 (G20 2020a). This was accompanied by specific commitments to “close the financing gap in the WHO Strategic Preparedness and Response Plan” and “provide immediate resources to the WHO’s COVID-19 Solidarity Response Fund, the Coalition for Epidemic Preparedness Innovations (CEPI) and Gavi, the Vaccine Alliance” (G20 2020a). One tally counted some 21 billion dollars 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 course of the year, and into the following year, including the

Declaration of G20 Health Ministers adopted in Rome in September 2021 (G20 2021).

4.2 Multilateral Responses from Diverse Sectors

In April 2020, shortly after the G20 meeting discussed above, a broad coalition of different partners assembled under the joint leadership of the European Commission, France and the WHO, to establish the Access to COVID-19 Tools Accelerator (ACT), which 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 non-governmental organizations (NGOs) such as the GAVI vaccine alliance, and the Coalition for Epidemic Preparedness Innovations (CEPI). By early 2022, COVAX had shipped over 1 billion vaccine doses to 144 countries, with 191 countries participating in the initiative (the vaccine distribution effort is discussed in more detail below). Another important feature of COVAX which distinguishes it from purely national approaches is the diversity of its vaccine portfolio. As GAVI itself 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).

4.3 The Race to Develop and Mass Produce a Vaccine

Much has been written about the unprecedented speed with which not just one, but several vaccines were successfully developed, approved and then mass-produced to counter COVID-19 (Tooze 2021). As one commentator notes, just six weeks after Chinese researchers published the genome of the virus, a U.S. biotechnology company was able to notify authorities of a new vaccine candidate for the purpose of conducting clinical trials, and as early as April 2 – and thus less than a month after the 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).

Under normal conditions, vaccine development generally takes about 10 to 15 years (The College of Physicians of Philadelphia 2018). Up until the COVID-19 vaccine, the fastest vaccine that had been developed was that for the mumps, which took 4 years (Cohen 2020, Solis-Moreira 2021). Given the catastrophic impact COVID-19 had from the earliest days of the pandemic, both on countries’ public health systems but also their economies and the social fabric of cities and communities around the world, it was imperative that a vaccine be found as soon as humanly possible. The WHO coordinated an international response that pooled information, allowed researchers to agree on the most promising candidates, and subsequently scale up clinical trials across multiple countries (United Nations Department of Global Communications [DGC] 2020, Voysey et al 2020). With applications being reviewed for different vaccine candidates by stringent NRAs such as the UK’s Medicines & Healthcare products Regulatory Agency (MHRA) and the FDA, the first emergency use authorizations started to be issued in December 2020.¹⁸ The WHO issued 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).

4.4 Making a Virtue out of Necessity through Regulatory Agility

The large amount of literature compiled since efforts to develop, test, approve and market a COVID-19 vaccine, documents the extraordinary and unprecedented degree to which NRAs chose to make a virtue of necessity and develop or expand upon regulatory agility to a degree never seen or even imagined before. For example Avorn and Kesselheim (2020) note that in June 2020, while announcing its expectation that any new vaccine “would reduce the occurrence or severity of disease in at least 50% of recipients” (and thus a success rate similar to that demanded of annual flu vaccines), the FDA also conceded that it might entertain “less conventional approaches,” one of which would be to allow for “accelerated approval” of a vaccine candidate, based not on the results of actual phase 3 clinical trials, but rather on the basis of “antibody levels or another biochemical marker” (Avorn and Kesselheim 2020, p. 1284). Ultimately the FDA authorized the Pfizer-BioNTech COVID-19 Vaccine on 11 December 2020 under an Emergency Use Authorization (EUA) on the basis of results from phase three trials involving 37,586 participants who were enrolled “in an ongoing randomized, placebo-controlled international study”, with the majority of these participants being in the United States (FDA 2020).

Another example of regulatory agility that resulted from the pandemic and which was aimed at the expedited regulatory approval of vaccines as they were rapidly being developed, was the formation within COVAX (discussed above), of a Regulatory Advisory Group (RAG), co-led by the WHO and the Coalition for Epidemic Preparedness Innovations (CEPI), comprising representatives from 10 NRAs from different countries and regions to deliberate upon and provide feedback with respect to vaccine development by different manufacturers.¹⁹ For example, in order for vaccine developers to obtain more coordinated feedback from NRAs, the RAG 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 2021d, p.2).

Yet another example of innovative approaches under the mantra of regulatory agility and which alleviated the burden on vaccine developers was in the area of 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” (ibid, p. 4), before a number of NRAs such as the EMA, the US FDA, Health Canada, HSA Singapore and TGA Australia developed additional processes including remote/virtual inspections (ibid).

Yet again among efforts to increase regulatory agility by increasing collaboration among regulators and once more under COVAX, was the establishment of Support Work to Advance Teams (SWAT) comprising groups of experts dedicated to “resolving technical issues and challenges common across all COVID-19 vaccine development projects” (McGoldrick, Gastineau, Wilkinson et al 2022, p. 1217). For example a Manufacturing SWAT was established with representatives from regional and global industry associa-

tions to focus on a number of 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, support for batch release testing (ibid).

These and numerous other examples show that as the scale of the pandemic took on proportions unprecedented in recent history, and both its health and economic effects became politically unbearable, regulators scrambled to pull out all the stops to rapidly test and approve new vaccines. However, it is also important to note that they did this while at the same time adhering to the highest standards of scientific rigor and medical safety. These standards had long been forming as part of regulatory collaboration initially between a small group of stringent NRAs, but which over time became broader and more inclusive and ultimately enjoyed the legitimacy afforded these efforts by their close association with organizations like the World Health Organization and multi-stakeholder initiatives like COVAX and CEPI.

NOTES

18 The UK MHRA granted temporary use approval for the Pfizer-BioNTech vaccine on 2 December 2020. The U.S. FDA issued an Emergency Use Authorization (EUA) on 11 December 2020.

19 The countries and regions from which representatives of 10 NRAs constituted the Regulatory Advisory Group were Argentina, Australia, Brazil, Canada, Europe (EMA and the European Directorate for the Quality of Medicines & Health Care - EDQM), Ghana, Japan, Singapore and USA.

Regulatory Cooperation and Vaccines in Asia Pacific

IN THIS SECTION

5.1 Reliance on WHO and SRAs

5.2 ADB financing and APVAX

5.3 ASEAN Initiatives

5.4 WHO regional networks

5.5 APEC

5.6 ESCAP

5.7 An Assessment

How reliance on WHO and stringent regulators, regional financing and regional networks shaped vaccine regulation across the region.

In the Asia-Pacific region, a number of initiatives are worth mentioning with regard to regulatory cooperation, both to mitigate the health and economic impacts of the pandemic and to promote regulatory agility in the approval and distribution of vaccines. Compared to other regions, Asia-Pacific has performed relatively well, both as a source of new vaccines and in successfully executing national vaccine rollouts.

At the level of distribution, the region played host to some of the countries that succeeded best in vaccinating a significant portion of their populations the fastest, such as Singapore, and – after initial stumbles – Australia.²⁰ Even some of the region's LDCs such as Cambodia succeeded in achieving remarkably high vaccination rates within a relatively short timeframe. But there are also more sobering statistics that attest to the varying degrees of success that have characterized governments' responses to COVID-19 across the region, with under-resourced public health systems and limited administrative capacity to navigate recurring outbreaks, as new variants of the virus emerged, posing challenges to a number of governments.

As this section will show, the most consequential form of regulatory cooperation in the region during the pandemic was not the product of any new regional institution, but rather of reliance – and predominantly unidirectional reliance at that (see Section 3.3.3). Most NRAs in the region lacked the capacity to

independently review the clinical trial data of novel vaccine candidates within the timeframe the crisis demanded, and chose instead to take their cue from the decisions of a small number of reference authorities. Regional institutions, for their part, played an important supporting role, whether by embedding reliance in the conditions attached to vaccine financing, by promoting the convergence of regulatory requirements over the longer term, or by facilitating the movement of vaccines and related goods across borders. Each of these dimensions is discussed in turn below.

5.1 Reliance on WHO and Stringent Regulatory Authorities

At the outset of the vaccine rollout, only two NRAs in the Asia-Pacific region, namely those of Australia and Japan, were counted among the stringent regulatory authorities recognized by the WHO (ADB 2021b). For the vast majority of the region's regulators, the decisions of SRAs such as the U.S. FDA, the EMA and the UK MHRA, together with the WHO's own Emergency Use Listing (EUL) procedure, thus became the reference points on the basis of which national emergency use authorizations were granted. As the ADB observed at the time, decisions taken by SRAs and the WHO enjoyed wide international acceptance and helped NRAs in many developing countries to expedite their own approval processes (ADB 2021b).

The country case studies in Annex II illustrate how this played out in practice. Cambodia granted emergency use approval to the AstraZeneca vaccine approximately a week after it had been listed by the WHO, while Vanuatu, which does not appear to possess the capacity to carry out independent approvals of its own, relies on the WHO altogether. Singapore, although itself home to one of the region's most sophisticated regulators, chose in August 2021 to recognize all vaccines on the WHO EUL for the purposes of conferring vaccinated status, and Australia likewise recognized a number of EUL-listed vaccines for the purposes of international travel that were not part of its own national rollout. In this sense, the WHO EUL came to function as a regional (and indeed global) reference standard, even for those NRAs that retained the capacity to reach their own decisions.

Importantly, reliance of this kind does not entail a surrender of regulatory sovereignty. As the WHO's Good Reliance Practices, adopted in 2021, make clear, the relying authority remains independent, responsible and accountable for the decisions it takes, even where these are informed by the assessments of others (WHO 2021e).²¹ The practical effect of reliance is rather to free up scarce national resources for those regulatory functions that no other authority can perform, such as pharmacovigilance, market surveillance and the oversight of local manufacturing and distribution – functions which, as discussed in Section 6, took on growing importance as countries moved from emergency authorization to mass rollout and post-market surveillance.

5.2 Financing Conditioned on Regulatory Standards: The Asian Development Bank

As a regional development bank with deep ties to and intricate knowledge of the Asia-Pacific region, as well as an established presence thanks to its in-country offices, the ADB was well placed to identify and address the most urgent problems confronting its developing member countries (DMCs) as the pandemic unfolded, with regard to both the public health and the economic impacts of the virus.

5.2.1 Asia Pacific Vaccine Access Facility (APVAX)

In December 2020, and thus just as the first emergency use authorizations were starting to be issued in the U.S. and the UK (and later in the month by the WHO), the ADB launched the Asia Pacific Vaccine Access Facility (APVAX) in response to the resource constraints faced by many of its DMCs (ADB 2020). The initiative was essentially a USD 9 billion financing facility comprising two core components: the first a rapid response element intended to provide quick access to diagnostic resources and vaccines; the second comprising financing and support for more long-term and systemic efforts to improve distribution, including transport, storage and administration, as well as institutional capacity building and post-market surveillance (ADB 2021a). As of September 2021, the ADB reported that it had committed a total of USD 20.8 billion to its COVID-19 response, including USD 2.3 billion under APVAX (ADB 2021c).

What makes APVAX particularly relevant for the purposes of the present discussion is that it embedded reliance directly into the conditions attached to vaccine financing. To be eligible for financing under the facility, a vaccine had to meet at least one of three criteria, namely that it be procured through COVAX, that it be prequalified by the WHO, or that it be authorized by a stringent regulatory authority (ADB 2020b). In this way, the ADB effectively extended the reach of SRA and WHO decisions to the procurement decisions of borrowing governments, without, however, displacing national authorization. In the case of Sri Lanka, for example, the relevant project documentation makes clear that, in addition to meeting one of the APVAX eligibility criteria, vaccines also had to be authorized by the country's own National Medicines Regulatory Authority (ADB 2021d). Financing, in other words, served as a vehicle for promoting reliance while leaving the formal authority of the national regulator intact.

5.3 ASEAN Initiatives

Efforts by ASEAN at closer regulatory cooperation in the area of medicines (and thus by extension vaccines) had long preceded the COVID-19 pandemic and had their roots in efforts to more closely integrate the different national economies to form a single regional market (Lätzel 2007). Below we discuss a number of

these initiatives in more detail and show how, as in other regions, the urgency of the pandemic led Member States to pursue national solutions rather than rely on regional mechanisms that had been designed for a different pace of work.

5.3.1 ASEAN Pharmaceutical Product Working Group (PPWG)

The PPWG was the result of broader efforts to eliminate technical barriers to trade under processes that were part of ASEAN's 1992 FTA, particularly those of its Consultative Committee on Standards and Quality (ACCSQ) (Lätzel 2007). The PPWG was established in 1999 to support two objectives. The first was the removal of technical barriers to trade in pharmaceutical products. The second was facilitating access to these products in ASEAN “without compromising” their “safety, efficacy and quality.”²²

Over the years, the PPWG has achieved some notable successes in areas such as harmonized requirements for the ASEAN Common Technical Dossier and the ASEAN Common Technical Requirements, as well as regional MRAs on GMP inspections (2009) and on Bioequivalence Study Reports of Generic Medicinal Products (2018). However, the reality immediately prior to 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).

5.3.2 ASEAN Joint Assessment Coordination Group

The JACG coordinates the ASEAN Joint Assessment procedure, a mechanism for streamlining approvals for pharmaceuticals across participating ASEAN Member States. The way the scheme essentially works is that a single marketing authorization application is simultaneously filed with all participating ASEAN NRAs, who then work collaboratively to produce a joint assessment report (HSA 2020). Although the ultimate aim of the procedure is to facilitate authorization and thus expedite access to medicines that are deemed to be safe, of high quality and efficacious, it is also very much a capacity building exercise in the spirit of the WHO's Regulatory System Strengthening (RSS) efforts. In order to qualify for the Joint Assessment procedure, a product must already have been approved by at least one SRA (generally the EMA or the U.S. FDA) or have been prequalified by the WHO, and must be

aimed at treating a priority disease in the ASEAN region (HSA 2020).

At the level of regulatory policy more broadly, the ASEAN-OECD Good Regulatory Practice Network (GRPN), which brings together officials responsible for regulatory policy and reform rather than medicines regulators as such, also met repeatedly during the pandemic, focusing on the changes to regulatory policy making associated with governments' responses to the crisis and on how better regulation reforms could support the recovery (OECD 2021b).

5.3.3 ASEAN Member States Embrace Regulatory Agility

Although leaders and policymakers in ASEAN Member States recognized how much had been achieved over the years by the gradual and painstaking collaborative efforts of pharmaceutical regulators meeting and working at the ASEAN level in processes like the PPWG and JACG described above, it was likewise clear that these mechanisms and processes were not a viable option for the kind of regulatory agility required in the face of the looming public health disaster that COVID-19 spelled for countries in the region. As a result, Member States pursued their own solutions for procuring and authorizing different vaccines for their populations. Given how differently ASEAN operates from the EU, which pools both sovereignty and resources to a far greater degree and took a supra-national approach to the procurement and rollout of vaccines, at least one commentator has argued that the approach taken by leaders and regulatory bodies in ASEAN was the correct one for the region (Lim 2021).

Indeed, the fact that each ASEAN Member State essentially opted for its own responses in terms of whether to close borders, the degree to which lockdowns and other social distancing measures were imposed and other emergency decisions taken to safeguard their own populations, is a testament to the extreme pressure governments were feeling in the early days of the pandemic. This was compounded by the fact that so little was initially known about the new virus (in terms of its nature and transmissibility) and that expectations at the outset were that a vaccine would take several 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 really no wonder that "urgent socio-political considerations [took] precedence over regional regulatory cooperation" (Lim 2021).

5.4 WHO-Supported Regional Regulatory Networks

Alongside ASEAN, WHO-supported networks have provided a further platform for promoting reliance in the region. The South-East Asia Regulatory Network (SEARN), established under the auspices of the WHO Regional Office for South-East Asia, brings together NRAs from across the WHO South-East Asia Region, which includes Bangladesh and India among the economies covered in the country case studies. Among its priority action points is a strategy to facilitate reliance, which builds explicitly on the WHO's Good Reliance Practices and envisages NRAs in the region drawing on the work of reference authorities, including WHO prequalification, when reaching their own decisions (SEARN n.d.). Networks of this kind are unlikely to produce the sort of binding arrangements discussed in Section 3.3, but they matter precisely because they institutionalize the practice of reliance among working-level regulators, which is where the trust on which all reliance depends is ultimately built.

5.5 Asia Pacific Economic Cooperation (APEC)

APEC's response to the COVID-19 pandemic was a combination of ministerial summitry, joint political declarations and technical best-practice guidelines to support member governments in managing different policy aspects of coping with and overcoming the various challenges the pandemic poses. These initiatives span a range of different 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 difficult and urgent decisions (APEC 2021).

5.5.1 APEC Life Sciences Innovation Forum

The APEC Life Sciences Innovation Forum (LSIF) was established in 2002 while Mexico was hosting APEC. The LSIF is a multi-stakeholder grouping that brings together representatives from government, industry

and academia, and its importance has grown over the years so that today it has become the leading platform for APEC in health and life sciences. Its mission is essentially threefold: (1) harmonization with international standards; (2) to promote technical cooperation with a view to building capacity; and (3) serving as a platform for public-private collaboration in the field of life sciences innovation (APEC LSIF, 2022).

In terms of its contribution to regulatory cooperation during the COVID-19 pandemic, it was under the auspices of the Forum's Regulatory Harmonization Steering Committee (RHSC) that much of this work was undertaken. Established in 2008 under the chairmanship of Health Canada, the RHSC had long been working towards regulatory convergence for approvals of medical products under a strategic framework, the target date for completion of which was – coincidentally enough – 2020 (ibid), with key performance indicators (KPIs) being adopted by the group in 2018 to measure convergence across four areas of best practices (Chong et al 2021).²³ Notably, one of these four areas is the use of risk-based evaluation based on reliance practices, which aligns the RHSC's agenda closely with the reliance dynamic described above.

5.5.2 APEC Regulatory Responses to Support Vaccine Distribution

One initiative, on Securing Access to COVID-19 Vaccines and other Medical Products, has culminated in a number of 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 send a strong signal to the global community that APEC is committed to expediting the successful rollout of COVID-19 vaccines" (APEC 2021), while the Toolkit is aimed at helping policymakers grapple with "areas of vulnerability in the medical product supply chain and the lifecycle of medical products", particularly with respect to sub-standard and falsified medical products (APEC 2021).

5.6 UN Economic and Social Commission for Asia and the Pacific (ESCAP)

As one of the five regional commissions of the United Nations, ESCAP has also risen to the challenge to offer its support to the region in various ways. One such way is the development of what it calls a “framework to support the socio-economic response of Asia and the Pacific to the COVID-19 pandemic” (ESCAP, 2020). 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 and can thus leverage these strengths with the urgency the situation demands. The three areas of work in question are: (1) protecting people and enhancing resilience; (2) supporting economic recovery; and (3) restoring supply chains and supporting small and medium-sized enterprises (SMEs) (ESCAP 2020).

Of particular relevance to the cross-border movement of vaccines and other medical products is ESCAP’s work on trade facilitation. The Framework Agreement on Facilitation of Cross-border Paperless Trade in Asia and the Pacific, a UN treaty negotiated under ESCAP’s auspices, entered into force in February 2021 and provides a platform for the cross-border recognition of trade-related data and documents in electronic form, including the kinds of certificates and permits that accompany shipments of medical products (ESCAP

2016). Although not an instrument of regulatory cooperation in the sense discussed in Section 3, it addresses precisely the kind of border frictions that the APEC guidelines discussed above sought to reduce, and could usefully be leveraged in future health emergencies.

5.7 An Assessment

Taken together, these initiatives suggest that regulatory cooperation in the Asia-Pacific region during the pandemic was characterized less by the creation of new mechanisms than by the rapid and pragmatic use of existing ones – and above all by reliance on the decisions of the WHO and a handful of stringent regulators. This allowed regulators with limited capacity to authorize vaccines within weeks rather than months, but it also exposed the extent to which the region remains dependent on reference authorities located, for the most part, outside it. The longer-term harmonization efforts pursued under ASEAN and APEC, although valuable, were not designed for the speed the crisis demanded and, as discussed above, were largely set aside in favor of national solutions. Entrenching the gains in regulatory agility achieved during the pandemic will thus require both strengthening the capacity of the region’s own regulators and placing reliance on a more deliberate and formal footing, themes to which the policy recommendations in Section 6 now turn.

NOTES

20 By mid-December 2021, Singapore had fully vaccinated some 87 percent of its total population, predominantly with either the Pfizer-BioNTech or the Moderna vaccine (Fortune 2021). In Australia, just over 91 percent of the population aged 16 and over had received two doses by the end of December 2021, with the AstraZeneca, Pfizer-BioNTech and Moderna vaccines being favoured by the national vaccine rollout (Australian Government Department of Health 2021).

21 The WHO defines reliance as the act whereby the regulatory authority in one jurisdiction takes into account and gives significant weight to assessments performed by another regulatory authority or trusted institution in reaching its own decision. The Good Reliance Practices were adopted by the WHO Expert Committee on Specifications for Pharmaceutical Preparations as an annex to its fifty-fifth report (WHO 2021e).

22 Article 1 of the PPWG’s Terms of Reference, available at: https://www.tisi.go.th/data/interstandard/pdf/asean/asean_ppwg_tor_2_6.pdf

23 These were: (1) The removal of the Certificate of Pharmaceutical Product (CPP); (2) The use of the Good Manufacturing Practices (GMP) certificate issued by the Pharmaceutical Inspection Cooperation Scheme (PIC/S) network; (3) The management of multiple manufacturing sites under a single license from the regulatory authority; (4) The use of risk-based evaluation based on reliance practices (Chang et al 2021, p. 2).

Outlook and Policy Recommendations

IN THIS SECTION

- 6.1 Urgency as Driver of Regulatory Agility
- 6.2 Some Tentative Lessons Learned
- 6.3 Policy Recommendations to Improve Regulatory Agility

The present outlook, tentative lessons learned, and five measures to improve regulatory agility.

RECOMMENDATIONS AT A GLANCE

Maintain publicly available and up-to-date lists of approved medicines

01

- PROBLEM** In many countries it is unclear which medicines are approved for public sale, owing to weak legislative mandates, poor accessibility or lists that are not maintained.
- ASK** Does the NRA already publish such a list, fully or partially? If not, is the obstacle legal authority, resources, or both?
- ACT** Delegate authority and allocate resources to the NRA to establish and maintain the list, using the WHO Model Lists of Essential Medicines as a starting template.

Mandate time-limits for NRAs to adopt and publish decisions

02

- PROBLEM** Approval delays driven by resource bottlenecks at the NRA.
- ACT** Study pandemic-era expedited practices, legislate binding time-limits, and require semi-annual reporting on compliance.

Prescribe the WHO Collaborative Registration Process for prequalified products

03

- PROBLEM** NRAs lacking capacity to assess complex clinical trial data.
- ACT** Run a cost-benefit study of participation, address constraints, and approach WHO on joining.

Adopt concrete steps to promote cooperation between NRAs

04

PROBLEM

Fragmented supply chains make cooperation essential, but political will and resources lag.

ACT

Map existing links, target capacity gaps, and agree terms with partner NRAs.

Implement a dedicated capacity building program for the NRA

05

PROBLEM

Upgraded capacity leaks to the private sector over time.

ACT

Prioritise cost-effective avenues such as twinning, placements and secondments with foreign NRAs.

6.1 Urgency as Driver of Regulatory Agility

The COVID-19 pandemic, despite the massive toll it has taken both in the loss of human life but also the devastating impact it has wreaked on livelihoods in many nations, and especially poor countries, 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). To be sure, the circumstances surrounding the pandemic were a so-called “once-in-a-hundred-year event” (Cruickshank and Shaban 2020)²⁴, and the urgency felt by governments in the face of the negative health impact, the socio-economic hardships, and the potential political instability these factors gave rise to, made discovering, approving, and delivering a vaccine one of the most complex and urgent imperatives governments have had to face so far this century. The implication is that this newfound regulatory agility was undoubtedly the result of intense political pressure.

Another important factor, no less related to the unique urgency of the situation, was – a certain degree of vaccine hesitancy notwithstanding – the relatively diminished risk-aversion of affected populations, particularly given the size of the unmet need when weighed against the obvious health and economic risks COVID-19 engendered. This confluence of factors meant that both political leaders and more importantly regulators understood and came to recognize that as a rule people were generally clamoring for a vaccine, both because it promised some degree of protection from many of the negative health impacts of COVID-19, but also because it was seen as the fastest way to end the lockdowns and secure a return to normal economic and social life. As such there was

greater risk tolerance for one or more vaccines that were new and without the many years of extensive clinical trial data (Mak et al 2020).

In many countries in the APAC region, like in Africa, 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 and certainly not within the timeframe required to mount an effective response to the unfolding crisis, with the notable exceptions of the NRAs of Australia, Japan, the Republic of Korea and Singapore, as well as the regulators in China and India, which authorized domestically developed vaccines on the basis of their own reviews. This crisis it should be remembered, proved more and more challenging to governments as the pandemic wore on, because of the emergence of new strains that were both more transmissible and – at least before the advent of the Omicron variant – similarly virulent, such as the Alpha, Beta and Delta variants (first identified in the United Kingdom, South Africa and India respectively). As such, NRAs were forced to make a virtue of necessity, and rely on the tried and trusted emergency authorization procedures of stringent regulatory authorities like the U.S. FDA and the EMA, as well as on the WHO’s own Emergency Use Listing (Soumyanarayanan et al 2021), with many if not all NRAs in the region choosing to follow the example set by one of these reference authorities.

By the beginning of 2022, the focus had shifted from regulatory cooperation in the approval of vaccines for emergency use, to other efforts such as 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 constantly mutating virus, and improving the exchange of information as countries

moved to the post-market surveillance stage and as the need arose to remain vigilant both for any new variants as well as any as yet undetected adverse drug reactions that could be statistically significant. There is also a desire to entrench to one degree or another, much of the progress made in regulatory agility during the crisis, particularly by drug companies and others pushing for greater access to medicines generally.

6.2 Some Tentative Lessons Learned

The COVID-19 pandemic represented a steep learning curve for political leaders across the world, who had to quickly learn to absorb and take decisions on advice from epidemiologists, virologists and other specialized medical experts, assisted by health policymakers. Some leaders proved more receptive to dealing with the technical complexities of the underlying phenomenon and in accepting the health advice given while others maintained or asserted varying degrees of adherence to politically expedient solutions or ideological positions. In the end, a number of factors including the soundness of the policy response, but also geographic, climatic, and demographic realities served to influence how successful countries were initially at flattening the curve and then later at procuring and rolling out vaccines.

Despite the high degree of uncertainty as to the nature of the virus in the first weeks and months, those countries which moved quickly to implement proven and well-understood infection prevention and control (IPC) measures, such as closing or at least carefully monitoring borders, imposing strict restrictions on the movement of persons across and within borders, and implementing testing and tracing protocols, proved the most successful at staving off disaster or at least rapidly curtailing smaller outbreaks as they occurred. As the virus evolved and mutated becoming more transmissible with each new variant and as lockdown fatigue among affected populations made restrictions on economic activity increasingly costly politically, many of the measures that governments had taken in the first wave proved insufficient in successive waves, particularly in the face of the more transmissible Delta - and then later - Omicron variants. The COVID-19 pandemic will have instilled many governments with a better understanding of which

restrictions impose the greatest cost economically and politically and how best to manage the cost-benefits calculus of restrictions and their potential benefit to the public health system versus their socio-economic impact on different elements of society.

Those countries which had pre-existing outbreak preparedness systems either in place or at the ready fared better than those without. In many instances, this was a function either of a country's previous exposure to similar outbreaks such as the 2003 SARS virus (China, Hong Kong, Singapore, and Vietnam) or other bureaucratically entrenched sensitivities to biosecurity threats (Australia and New Zealand). Interestingly, the 2019 Global Health Security Index, which assessed the health security capacities of some 195 countries, ranked the United States and the United Kingdom as the best prepared, a finding that was soon proven to be misplaced. However, one finding contained in the GHS Index that proved prescient was the following:

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. (Cameron et al 2019, at p. 9)

No doubt, after COVID-19, outbreak preparedness will be a policy priority for many governments throughout the world for years to come. Indeed, the laboratory capacity China had built up since SARS allowed its scientists to sequence the virus within weeks and share the genome with the world, although the handling of the earliest phase of the outbreak, including delays in alerting the international community, remains contested (Independent Panel for Pandemic Preparedness and Response 2021). Likewise, it was Singapore's outbreak preparedness and the protocols put in place following SARS that allowed it quickly to mobilize and organize effective decision-making at the very highest level of political leadership and have a dedicated task force up and running within days of the first reports of the mysterious new virus detected in Wuhan (see Singapore case study).

Yet another lesson that has been learned is the importance of achieving universal vaccination across all

countries. Of course, a lot of lip service was paid by developed and developing countries on the need to avoid vaccine nationalism and to ensure vaccine equity between rich and poor. But when supplies looked like they were becoming constrained as they did at several junctures, national governments in producing countries did what their domestic populations demanded, which was to prioritise the needs of their own citizens first. There was also a good deal of vaccine hoarding by developed countries over the course of 2021 (Nebehay and Mason 2021). However, the recurring emergence and spread of new and more transmissible variants, such as the Beta and Omicron variants (first identified in South Africa) and the Delta variant (first identified in India) drove home the need to vaccinate the entire world, and that doing so as soon as possible is in the self-interest of all countries, rich and poor, if the world is to finally be able to put the health risks, economic instability and disruption of daily life due to the COVID-19 crisis behind it.

6.3 Policy Recommendations to Improve Regulatory Agility

The policy recommendations provided below seek to support governments and public health authorities in improving the regulatory agility of NRAs to better execute their mandate to uphold the three pillars of modern medicines regulation in ensuring the quality, safety and efficacy, of medicines through their various activities, including in particular the “licensing, control and monitoring of the manufacture, import, export, distribution, promotion, and advertising of medicines; assessing the safety, efficacy, and quality of medicines; and inspection and surveillance along the entire supply chain”. (Bell, 2016).

6.3.1 Maintain Publicly Available and Up-to-date Lists of Approved Medicines

This may not be necessary in countries with a well-regulated and adequately financed public health system, but in many countries transparency deficits as to what medicines have been approved for public sale is still lacking or may be insufficiently communicated. This can be due to a variety of factors, including 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, nor is it maintained in a format that is

amenable to regular updates that can be easily disseminated to the broader public.

To properly address this issue, public health authorities need to ask a number of questions, including whether this is something the NRA already does in a comprehensive or partial manner and if this is not being done, why, i.e., is this due to a lack of legislative and regulatory authority, or resource constraints or both?

As part of efforts to improve transparency around public health, and as part of 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 catalogue different medicines).

6.3.2 Mandate Time-Limits for NRAs to Adopt and Publish Regulatory Decisions

The long delays that can ensue in the course of seeking and obtaining regulatory approvals are a common complaint for the pharmaceutical industry, although in some cases this can be due to issues beyond the NRA’s controls, such as the integrity of clinical trial data. In other cases, resource constraints at the NRA will be the key bottleneck, a problem that can admittedly only be fixed with the necessary political will, but is also contingent on outside technical assistance and support.

Here, the process of remedying systemic delays begins with asking the right kind of questions, such as how long does it currently take for the NRA to adopt and publish regulatory decisions in the context of approval procedures? Also, is the current time required in line with those required by NRAs in countries at similar levels of economic development? Also helpful in this regard is an answer to the question of whether the COVID-19 pandemic resulted in the adoption and publication of regulatory decisions at a more expedited rate than has generally been the case prior to 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 in response to the urgent need to approve one or more COVID-19

vaccines? Once these questions have been asked, the next logical question is what additional resources or authorizations would the NRA require in order to adopt such expediciencies on a permanent basis?

As alluded to above, achieving permanent efficiency gains in the work processes of regulatory bodies requires both the political will and the administrative capacity to do a post-mortem of how the NRA expedited approvals during the COVID-19 pandemic and which innovations could be permanently adopted in future without compromising the NRA's core mission.

To do this, governments should carry out a study of time limits for the adoption and publication of regulatory decisions prior to and during the COVID-19 pandemic, identifying which innovations the NRA adopted to expedite the approval of COVID-19 vaccines. In addition to this, governments seeking to institutionalize any innovative expediciencies achieved in response to COVID-19 will need to legislate the adoption of those innovations that can be permanently adopted without compromising the NRA's core mission, setting binding time limits for NRAs to adopt and publish regulatory decisions. This also requires appropriating and allocating sufficient resources as are necessary to support the NRA in the implementation of these new requirements.

For the purposes of accountability and in order to benchmark any progress made, governments should also require that the NRA provide a semi-annual accounting of its success or failure in adhering to these new time-limits, with any failures being accompanied by reasons for their occurrence and internal recommendations for how such failures can be avoided in future.

6.3.3 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 and detailed approval procedures. In many countries, the main obstacles to participation are likely to be either of a political-economy nature (i.e., existing market participants are more satisfied with the status quo), related to govern-

ment concerns over a real or perceived diminution in regulatory sovereignty that joining the procedure may entail, or be due to resource constraints. In other cases, where regulatory capacity is already deemed sufficiently robust, this may seem unnecessary.

Questions that are useful in clarifying the need to adopt this recommendation include is the NRA currently participating in the scheme?²⁵ If it is not participating, what are the main hurdles to participation? Finally, governments need to ask whether there would be considerable benefits to the main stakeholders of the country's public health sector (consumers, medical practitioners, hospitals, medical insurers) in joining the scheme?

In this context, it is recommended that governments initiate a study on the costs/benefits of participating in the scheme and identify what the relevant constraints are. If the government can demonstrate that the benefits outweigh the costs and can overcome any identified constraints, approach the WHO on joining the scheme, which is more than willing to offer countries advice on how to go about doing this.

6.3.4 Adopt Concrete Steps to Promote Cooperation between NRAs

As noted previously throughout this paper, in the modern world of complex and fragmented pharmaceutical supply chains, cooperation between different NRAs is becoming not just desirable but essential, something that the pandemic demonstrated all too visibly. The main challenges to doing this lie in garnering sufficient political will on the part of participating governments, but also identifying and allocating sufficient resources.

The questions governments need to be asking themselves in this regard are to what extent is cooperation between the country's NRA and more advanced NRAs already taking place either under regional cooperation arrangements or at the WHO? Also important to ascertain in this context is which NRAs in which countries would be the likeliest partners and would yield the best results in terms of different forms of cooperation over different time horizons?

Here it is recommended that the government first identify which forms of regulatory cooperation already exist with which foreign NRAs either in the region or at similar levels of maturity. Next, the gov-

ernment should identify those 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 happening. Following this, it is recommended that the government seeking to upgrade its own medical regulatory capacity approach the governments of the foreign NRAs with which greater cooperation is sought and agree upon the terms and conditions subject to which such cooperation shall take place (MOU, MRA, etc.). Finally, secure and allocate sufficient resources to the development and implementation of such regulatory cooperation initiatives, if necessary, by approaching relevant donor organizations.

6.3.5 Define and Implement a Dedicated Capacity Building Program for the NRA

The pathways for improving the capacity of country's public health regulatory authorities are by now quite well understood and the WHO among others has an established track record of doing just this in countries like Bangladesh, Rwanda, and Vietnam. This is first and foremost a resource issue, but also involves challenges of retaining any upgraded capacity over the medium to long term, which is a perennial problem for all capacity building efforts.

These efforts begin by asking what is the most cost-effective and impactful way in which capacity can be

built in the short to medium term? It is also helpful to clarify whether this would require large infusions of new resources and qualified staff and if so, how can such resources be secured (public budget and private sector contributions)? Also important from a human resource development perspective is the question of whether short-term improvements to resourcing and staffing are sustainable over time to avoid "leakage" of any upgraded human capacity to the private sector?

In terms of recommended measures to achieve this goal these include identifying which weaknesses in capacity are the most amenable to improvement over the short, medium and long terms. As well as identifying which avenues for capacity building are likely to be the most impactful and cost-effective (inhouse training, staff placements in foreign NRAs, secondments of staff from foreign NRAs, etc.). Governments are also advised to identify which foreign NRAs and other institutions can support them in their efforts to upgrade the capacity of their own NRA, through institutional twinning programs and similar efforts. Finally, it will be necessary to seek the help of capacity building experts in the field of regulatory approval of medicines at organizations like the WHO or stringent NRAs to support the government in drawing up and implementing its capacity building program.

NOTES

24 Cruickshank and Shaban (2020) pointedly note that "[while] the speed and consequences of the COVID-19 pandemic may seem to have come out of nowhere, for those who work in infection prevention and control (IPC), it comes as no surprise or shock".

25 We note that some APAC NRAs are already participating in this scheme, such as Bangladesh, Bhutan, Laos, Malaysia, Philippines and Thailand; see: <https://extranet.who.int/pqweb/medicines/collaborative-registration-faster-registration>.

Concluding Remarks

Closing reflections on readiness for the next pandemic.

It was thanks to the extensive and deep-rooted ways in which the world has grown intricately interconnected that the novel betacoronavirus SARS-CoV-2 was able to spread so rapidly and infect millions of people in virtually every country of the world in such a short period of time. But it was also thanks to a wide range of formal and informal cooperation arrangements and linkages that scientists, public health officials, regulators, and political leaders from all over the world were able to unite behind the common cause of defeating the virus and restoring the world and the global economy to some semblance of normality.

This paper has focused primarily on the way governments successfully cooperated to expedite the approval and rollout of an initial set of vaccines developed in countries such as the United States, the United Kingdom, China and India. This was without doubt the fastest example in human history of such an effort and has proven yet again the resourcefulness and doggedness of the human spirit and what

mankind is capable of when it unites its resources to achieve an identified goal.

However, the level at which governments cooperated during the pandemic went far beyond the narrow objective of developing and distributing vaccines. Governments worked together across a range of different regulatory areas to exchange information and share experiences on what measures were proving the most effective across a range of challenging policy problems both related to public health but also the equally important goal of protecting the vulnerable from the many socio-economic deprivations that social-distancing and other IPC measures gave rise to.

As the fight against the pandemic continues, albeit with an increasingly broad and sophisticated range of medical responses and policy tools, governments of all countries would be well advised to catalog and internalize the many lessons learned over the last two years, to better prepare themselves, their populations and their economies against future tests and crises.

References and Further Reading

Works Cited

- Aizenman, N. (2021, December 21). *The goal: at least 40% vaxxed in all nations by year-end. This map shows how we stand*. Retrieved from NPR: <https://www.npr.org/sections/goatsandsoda/2021/12/30/1068920127/the-goal-at-least-40-vaxxed-in-all-nations-by-year-end-this-map-shows-how-we-sta>
- Akhtar, M. (2022, January 13). *Is Covax finally going to vaccinate the world?* Retrieved from VOX: <https://www.vox.com/future-perfect/22872438/covax-omicron-covid-19-vaccine-global-inequity>
- ASEAN Business Staff. (2020, September 7). *Southeast Asia's GDP growth to contract by 4.2% in 2020; Vietnam recovery prospects brightest: ICAEW*. Retrieved from The Business Times: <https://www.businesstimes.com.sg/asean-business/southeast-asias-gdp-growth-to-contract-by-42-in-2020-vietnam-recovery-prospects-1>
- Asian Development Bank (ADB). (2020). *ADB's Support to Enhance COVID-19 Vaccine Access*. Manila (PH): ADB. Retrieved from <https://www.adb.org/sites/default/files/institutional-document/662801/adb-support-covid-19-vaccine-access.pdf>
- Asian Development Bank (ADB). (2016). *Better Regulation of Medicines Means Stronger Regional Health Security*. Manila (PH): ADB. Retrieved from [adb.org/sites/default/files/publication/184392/better-regulation-medicine.pdf](https://www.adb.org/sites/default/files/publication/184392/better-regulation-medicine.pdf)
- Asian Development Bank (ADB). (2020, December 11). *\$9 Billion ADB Facility to Help Developing Member Countries Access and Distribute COVID-19 Vaccines*. Retrieved from Asian Development Bank: <https://www.adb.org/news/9-billion-adb-facility-help-members-access-and-distribute-covid-19-vaccines>
- Asian Development Bank (ADB). (2021). *Getting Ready for the COVID-19 Vaccine Rollout*. Manila (PH): ADB. Retrieved from <https://www.adb.org/publications/getting-ready-covid-19-vaccine-rollout>
- Asian Development Bank (ADB). (2022, January 4). *Q&A on ADB's COVID-19 Assistance to Thailand*. Retrieved from Asian Development Bank: <https://www.adb.org/news/features/qa-ADB-covid-19-assistance-thailand>
- Asian Development Bank (ADB). (2021). *Responsive COVID-19 Vaccines for Recovery Project under the Asia Pacific Vaccine Access Facility (Sri Lanka): Vaccine Regulatory Approval (Supplementary Document)*. Manila (PH): ADB. Retrieved from <https://www.adb.org/sites/default/files/linked-documents/55085-001-sd-05.pdf>
- Asian Development Bank (ADB). (2021, September 13). *ADB's COVID-19 response for developing Asia surpasses \$20 billion*. Retrieved from Asian Development Bank: <https://www.adb.org/news/features/adb-covid-19-response-developing-asia-surpasses-20-billion>
- Australian Department of Health. (2022, January 17). *COVID-19 Vaccine Roll-out Update*. Retrieved from Australian Department of Health: <https://www.health.gov.au/sites/default/files/documents/2022/01/covid-19-vaccine-rollout-update-17-january-2022.pdf>
- Australian Government Department of Health. (2021, December 29). *COVID-19 Vaccine Rollout Update – 29 December 2021*. Canberra (AU): Department of Health. Retrieved from <https://www.health.gov.au/sites/default/files/documents/2021/12/covid-19-vaccine-rollout-update-29-december-2021.pdf>
- Avorn, J., & Kesselheim, A. (2020). Regulatory Decision-making on COVID-19 Vaccines During a Public Health Emergency. *Journal of the American Medical Association*, 1284–1285.
- Ballentine, C. (1981). Taste of Raspberries, Taste of Death: The 1937 Elixir Sulfanilamide Incident. *FDA Consumer Magazine*. Retrieved from <https://www.fda.gov/files/about%20fda/published/The-Sulfanilamide-Disaster.pdf>
- Bari, R., & Sultana, F. (2021). Second Wave of COVID-19 in Bangladesh: An Integrated and Coordinated Set of Actions Is Crucial to Tackle Current Upsurge of Cases and Deaths. *Front. Public Health*. doi:<https://doi.org/10.3389/fpubh.2021.699918>
- Berkley, S. (2020, September 03). *COVAX explained*. Retrieved from GAVI The Vaccine Alliance: <https://www.gavi.org/vaccineswork/covax-explained>
- Bhatia, U. (2020, December 23). *Vaccine Multilateralism – Singapore's Approach Towards Fair and Equitable Access for COVID-19 Vaccines*. Retrieved from Singapore Ministry of Foreign Affairs: <https://www.mfa.gov.sg/Newsroom/Press-Statements-Transcripts-and-Photos/2020/12/20201223-Op-ed-Amb-Umej-Bhatia>
- Bolislis, W. R., Lucia de Lucia, M., & Dolz, F. (2021). Regulatory Agilities in the Time of COVID-19: Overview, Trends and Opportunities. *Clinical Therapeutics*, 124–139.
- Bradley, J. (2020, April 09). *In Scramble for Coronavirus Supplies, Rich Countries Push Poor Aside*. Retrieved from New York Times: <https://www.nytimes.com/2020/04/09/world/coronavirus-equipment-rich-poor.html>
- British Broadcasting Corporation (BBC). (2021, December 28). *Covovax and Corbevax: What we know about India's new Covid vaccines*. Retrieved from BBC News: <https://www.bbc.com/news/world-asia-india-55748124>
- Brown, F. Z., Brechenmacher, S., & Carothers, T. (2020, April 06). *How Will the Coronavirus Reshape Democracy and Governance Globally?* Retrieved from Carnegie Endowment for International Peace: <https://carnegieendowment.org/2020/04/06/how-will-coronavirus-reshape-democracy-and-governance-globally-pub-81470>
- Cameron, E. E., Nuzza, J. B., & Bell, J. A. (2019). *Global Health Security Index: Building Collective Action and Accountability*. Washington (DC): The Nuclear Threat Initiative =.

- Campbell, C. (2020, August 24). *Exclusive: The Chinese Scientist Who Sequenced the First COVID-19 Genome Speaks Out About the Controversies Surrounding His Work*. Retrieved from Time: <https://time.com/5882918/zhang-yongzhen-interview-china-coronavirus-genome/>
- Chong, S. S., Kim, M., & Lim di, M. (2021). Measuring Progress of Regulatory Convergence and Cooperation Among Asia-Pacific Economic Cooperation (APEC) Member Economies in the Context of the COVID19 Pandemic. *Therapeutic Innovation & Regulatory Science*. doi:<https://doi.org/10.1007/s43441-021-00285-w>
- Clark, H. (2021, October 13). *Vietnam had seemingly conquered Covid. Then Delta spread*. Retrieved from The Interpreter: <https://www.lowyinstitute.org/the-interpreter/vietnam-had-seemingly-conquered-covid-then-delta-spread>
- Cohen, S. (2020, December 10). *The Fastest Vaccine in History*. Retrieved from UCLA Health: <https://connect.uclahealth.org/2020/12/10/the-fastest-vaccine-in-history/>
- Cruikshank, M., & Shaban, R. Z. (2020). COVID-19: Lessons to be learnt from a once-in-a-century global pandemic. *Journal of Clinical Nursing*. doi:<https://doi.org/10.1111/jocn.15365>
- Daemrich, A. (2009). *Where is the Pharmacy to the World? International Regulatory Variation and Pharmaceutical Industry Location*. Cambridge (MA): Harvard Business School.
- Das, K. N. (2021, December 15). *India stuck with COVID-19 vaccines it can't export*. Retrieved from Reuters: <https://www.reuters.com/world/india/india-stuck-with-covid-19-vaccines-it-cant-export-2021-12-14/>
- Dolgin, E. (2021). The tangled history of mRNA vaccines. *Nature*, 318–324.
- Duckett, S. (2021, April 01). *4 ways Australia's COVID vaccine rollout has been bungled*. Retrieved from The Conversation: <https://theconversation.com/4-ways-australias-covid-vaccine-rollout-has-been-bungled-158225>
- Dukes, M. (1986). The Regulation of Drugs: Worlds of Difference. *International Journal of Technology Assessment in Health Care*, 629–636.
- Ebbighausen, R. (2020, April 16). *How Vietnam is winning its 'war' on coronavirus*. Retrieved from DW: <https://www.dw.com/en/how-vietnam-is-winning-its-war-on-coronavirus/a-52929967>
- Encyclopædia Britannica. (2021, January 10). *Drug regulation and approval*. Retrieved from Britannica: <https://www.britannica.com/technology/pharmaceutical-industry/Drug-regulation-and-approval>
- European Commission. (2020). *Communication from the European Commission: EU Strategy for COVID-19 vaccines*. Brussels (BE): European Commission.
- European Medicines Agency. (2019). *From laboratory to patient: the journey of a centrally authorised medicine*. Amsterdam (NL): European Medicines Agency.
- Felter, C. (2021, December 27). *A Guide to Global COVID-19 Vaccine Efforts*. Retrieved from Council on Foreign Relations: <https://www.cfr.org/backgrounder/guide-global-covid-19-vaccine-efforts>
- Food and Drug Administration. (2018, September 06). *IDE Institutional Review Boards (IRB)*. Retrieved from U.S. Food and Drug Administration: <https://www.fda.gov/medical-devices/investigational-device-exemption-ide/ide-institutional-review-boards-irb>
- Food and Drug Administration (FDA). (2015, August 24). *FDA's Drug Review Process: Continued*. Retrieved from U.S. Food and Drug Administration: <https://www.fda.gov/drugs/information-consumers-and-patients-drugs/fdas-drug-review-process-continued>
- Food and Drug Administration (FDA). (2017, November 24). *The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective*. Retrieved from U.S. Food and Drug Administration: <https://www.fda.gov/drugs/information-consumers-and-patients-drugs/fdas-drug-review-process-ensuring-drugs-are-safe-and-effective>
- Food and Drug Administration (US). (2021, February 02). *Investigational New Drug (IND) Application*. Retrieved from U.S. Food and Drug Administration: <https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application>
- Food and Drug Agency (FDA). (2020, December 11). *FDA Takes Key Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for First COVID-19 Vaccine*. Retrieved from U.S. Food and Drug Administration: <https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19>
- Fortune. (2021, December 15). *Singapore plans to only consider those with boosters to be 'fully vaccinated'*. Retrieved from Fortune: <https://fortune.com/2021/12/15/singapore-fully-vaccinated-mandate-three-doses-booster-covid-omicron/>
- G20. (2020, March 27). *G20 Leaders' Statement Extraordinary G20 Leaders' Summit Statement on COVID-19*. Retrieved from reliefweb (United Nations Office for the Coordination of Humanitarian Affairs - OCHA): <https://reliefweb.int/report/world/g20-leaders-statement-extraordinary-g20-leaders-summit-statement-covid-19>
- Golberg, E. (2020, April 27). *Regulatory Cooperation to Combat Public Health Crises*. Retrieved from The Regulatory Review: <https://www.theregreview.org/2020/04/27/golberg-regulatory-cooperation-combat-public-health-crises/>
- Goldberg, E. (2019, June 17). *Giving Regulatory Cooperation a Reality Check*. Retrieved from The Regulatory Review: <https://www.theregreview.org/2019/06/17/golberg-giving-regulatory-cooperation-reality-check/>
- Goldberg, E. (2019). *Regulatory Cooperation – A Reality Check*. Cambridge (MA): Massavar-Rahmani Center for Business & Government at The Harvard Kennedy School.
- Gough, S. (2005). Post-marketing surveillance: a UK/European perspective. *Current Medical Research and Opinion*, 565–570.
- Graff, G. (2017). *Raven Rock: The Story of the U.S. Government's Secret Plan to Save Itself—While the Rest of Us Die*. New York (NY): Simon & Schuster.
- Griffin, J. P. (2004). Venetian treacle and the foundation of medicines regulation. *British Journal of Clinical Pharmacology*, 317–325.
- G20. (2021, September 7). *Declaration of the G20 Health Ministers*. Retrieved from Ministry of Health (Italy): https://www.salute.gov.it/imgs/C_17_pagineAree_5459_8_file.pdf
- Health Sciences Authority (HSA) Singapore. (2020, October 15). *ASEAN Joint Assessment Procedure for Pharmaceutical Products Information for Applicants*. Retrieved from Health Sciences Authority: https://www.hsa.gov.sg/docs/default-source/gdo/international-collaboration/asean/asean-jap-procedure-for-pharmaceutical-products-information-for-applicants_revised-as-of-5th-jacg.pdf
- Health Services Authority (HSA). (2020, December 04). *Access Consortium statement on COVID-19 vaccines evidence*. Retrieved from Health Sciences Authority: <https://www.hsa.gov.sg/therapeutic-products/international-collaboration/access/statement-on-covid-19-vaccines-evidence>
- Holbein, B. (2009). Understanding FDA regulatory requirements for investigational new drug applications for sponsor-investigators. *Journal of Investigative Medicine*, 689–94.

- Howes, S., & Surandiran, S. (2021, August 5). *Vanuatu: taking the pandemic in its economic stride*. Retrieved from Devpolicyblog: <https://devpolicy.org/vanuatu-taking-the-pandemic-in-its-economic-stride-20210805/>
- Imran, M., Najmi, A. K., & Rashid, M. F. (2013). Clinical research regulation in India-history, development, initiatives, challenges and controversies: Still long way to go. *Journal of Pharmacy & Bioallied Sciences*, 2–9.
- Independent Panel for Pandemic Preparedness and Response. (2021). *COVID-19: Make it the Last Pandemic*. Geneva (CH): The Independent Panel for Pandemic Preparedness and Response.
- International Coalition of Medicines Regulatory Authorities (ICMRA). (2021, December 31). Retrieved from International Coalition of Medicines Regulatory Authorities Website: <https://www.icmra.info/>
- International Council on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH). (2021, January 10). *ICH Guidelines*. Retrieved from ICH Harmonisation for Better Health: <https://www.ich.org/page/ich-guidelines>
- John, T. J. (2010). India's National Technical Advisory Group on Immunisation. *Vaccine*, 88–90.
- Karp, P. (2021, January 7). *Australia to roll out Covid vaccine in February, with goal for 4m jabs by March*. Retrieved from The Guardian: <https://www.theguardian.com/society/2021/jan/07/australia-to-roll-out-covid-vaccine-in-february-with-goal-for-four-million-jabs-by-march>
- Kevin Yaq, & Crossley, G. (2020, December 15). *China's factory recovery steps up as export, consumer demand grows*. Retrieved from Reuters: <https://www.reuters.com/article/us-china-economy-activity/chinas-november-industrial-output-steps-up-as-recovery-gathers-pace-idINKBN28P07C>
- Khadem, A. (2019). *WHO Regulatory Systems Strengthening Programme: WHO role in building effective and efficient regulatory systems for health products*. Retrieved from World Health Organization: https://www.who.int/medicines/technical_briefing/tbs/TBS2019_WHO_Regulatory_Systems_Building_GBT.pdf
- Khan, S., & Dhama, K. (2021). India's role in COVID-19 vaccine diplomacy. *Journal of Travel Medicine*. doi:<https://doi.org/10.1093/jtm/taab064>
- Khmer Times. (2021, July 16). *PM announces that 2 million 12-17 year olds will receive vaccine in Cambodia before schools reopen*. Retrieved from Khmer Times: <https://www.khmertimeskh.com/50894995/pm-announces-that-2-million-12-17-year-olds-will-receive-vaccine-in-cambodia-before-schools-reopen/>
- Khmer Times. (2021, November 15). *List of COVID-19 vaccines recognised by Cambodia for quarantine free international entry*. Retrieved from Khmer Times: <https://www.khmertimeskh.com/50971131/list-of-covid-19-vaccines-recognised-by-cambodia-for-quarantine-free-international-entry/>
- KPMG. (2020, November 18). *Australia: Government and institution measures in response to COVID-19*. Retrieved from KPMG: <https://home.kpmg/xx/en/home/insights/2020/04/australia-government-and-institution-measures-in-response-to-covid.html>
- Kunthea, M. (2021, November 1). *PM declares Cambodia fully reopen from Nov 1*. Retrieved from Phom Penh Post: <https://www.phnompenhpost.com/national/pm-declares-cambodia-fully-reopen-nov-1>
- Lesko, L. J., & Woodcock, J. (2004). Translation of pharmacogenomics and pharmacogenetics: a regulatory perspective. *Nature*, 763–769.
- Lim, J. C. (2021, April 15). *Wither ASEAN Regulatory Agility and Convergence in the Ongoing COVID-19 Pandemic?* Retrieved from SingHealth Duke-NUS Global Health Institute: <https://www.duke-nus.edu.sg/sdghi/resources/knowledge-centre/whither-asean-regulatory-agility-and-convergence-in-the-ongoing-covid-19-pandemic>
- Lindström-Gommers, L., & Mullin, T. (2019). International Conference on Harmonization: Recent Reforms as a Driver of Global Regulatory Harmonization and Innovation in Medical Products. *Clinical Pharmacology and Therapeutics*, 926–931.
- Liu, K. (2021). COVID-19 and the Chinese economy: impacts, policy responses and implications. *International Review of Applied Economics*, 308–330.
- Low, J. (2020, June 3). *COVID-19 Crisis Management: An Early Look*. Retrieved from Civil Service College Singapore: <https://www.csc.gov.sg/articles/covid-19-crisis-management-an-early-look>
- Lätzel, R. (2007). *Development of the ASEAN Pharmaceutical Harmonisation Scheme – An Example of Regional Integration*. Bonn (DE): Rhenish Friedrich Wilhelm University of Bonn. Retrieved from https://www.dgra.de/media/pdf/studium/masterthesis/master_laetzel_r.pdf
- Mahmud, F. (2021, April 1). *Bangladesh sees record high daily coronavirus cases amid surge*. Retrieved from Aljazeera: <https://www.aljazeera.com/news/2021/4/1/bangladesh-witnesses-a-record-surge-in-coronavirus-cases>
- Mallapaty, S. (2021, June 09). *China is vaccinating a staggering 20 million people a day*. Retrieved from Nature: <https://www.nature.com/articles/d41586-021-01545-3>
- McGarry, D. (2021, February 26). *Vanuatu coronavirus vaccine rollout to take until end of 2023*. Retrieved from The Guardian: <https://www.theguardian.com/world/2021/feb/26/vanuatu-coronavirus-vaccine-rollout-to-take-until-end-of-2023>
- McGinley, J., & Higgins, S. (2021). *Vaccination Nation: Unmasking Cambodia's Vaccination Success*. Bangkok (TH): Mekong Strategic Policy Capacity Building. GBT.pdf
- McGoldrick, M., Gastineau, T., & Wilkinson, D. (2022). How to accelerate the supply of vaccines to all populations worldwide? Part I: Initial industry lessons learned and practical overarching proposals leveraging the COVID-19 situation. *Vaccine*, 1215–1222.
- Ministry of Health Singapore. (2021, August 23). *Update on Local COVID-19 Situation and Vaccination Progress*. Retrieved from Ministry of Health: https://www.moh.gov.sg/newsroom/update-on-local-covid-19-situation-and-vaccination-progress_23_august_2021/
- Mohamadi, M., Lin, Y., Vuillet, M., Flahault, A., Rozanova, L., & Fabre, G. (2021). COVID-19 Vaccination Strategy in China: A Case Study. *Epidemiologia* 2021, 402–425.
- National Academies of Sciences, Engineering, and Medicine (NASEM). (2020). *Regulating medicines in a globalized world: The need for increased reliance among regulators*. Washington (DC): The National Academies Press.
- Ndomondo-Sigonda, M., Miot, J., Naidoo, S., Masota, N. E., Ng'andu, B., Ngum, N., & Kaale, &. (2021). Harmonization of medical products regulation: a key factor for improving regulatory capacity in the East African Community. *BMC Public Health*. doi:<https://doi.org/10.1186/s12889-021-10169-1>
- Nebehay, S., & Mason, J. (2021, December 10). *Reuters*. Retrieved from WHO warns against vaccine hoarding as poorer countries go without: <https://www.reuters.com/business/healthcare-pharmaceuticals/who-warns-against-vaccine-hoarding-poor-countries-go-without-2021-12-09/>

- Nikkei Asia. (2021, March 8). *Vietnam begins COVID vaccinations with AstraZeneca shots*. Retrieved from Nikkei Asia: <https://asia.nikkei.com/Spotlight/Coronavirus/COVID-vaccines/Vietnam-begins-COVID-vaccinations-with-AstraZeneca-shots>
- Nolte, D. (2022, February 01). *Relativizing the success of China's "vaccine diplomacy"*. Retrieved from German Council on Foreign Relations: <https://dgap.org/en/research/publications/relativizing-success-chinas-vaccine-diplomacy>
- Norberg, J. (2020). *Open: The Story of Human Progress*. London (UK): Atlantic Books.
- Olsson, S., Pal, S. N., Stergachis, A., & Couper, M. (2010). Pharmacovigilance Activities in 55 Low- and Middle-Income Countries. *Drug Safety*, 689–703.
- Organization for Economic Cooperation and Development. (2021, October 11). *Regulatory responses to the COVID-19 pandemic in Southeast Asia*. Retrieved from OECD: <https://www.oecd.org/coronavirus/policy-responses/regulatory-responses-to-the-covid-19-pandemic-in-southeast-asia-b9587458/#en dn otea0z3>
- Organization for Economic Cooperation and Development OECD). (2020, June 98). *No policy maker is an island: the international regulatory co-operation response to the COVID-19 crisis*. Retrieved from OECD: <https://www.oecd.org/coronavirus/policy-responses/no-policy-maker-is-an-island-the-international-regulatory-co-operation-response-to-the-covid-19-crisis-3011ccdd/>
- Organization for Economic Development and Cooperation (OECD). (2021, 12 15). *ASEAN-OECD Good Regulatory Practice Network*. Retrieved from OECD: <https://www.oecd.org/gov/regulatory-policy/asean-oecd-good-regulatory-practice-network.htm>
- Pan American Health Organization (PAHO). (2019). *Regulatory Reliance Principles: Concept Note and Recommendations*. Washington (DC): Pan American Health Organization.
- Pezzola, A., & Sweet, C. M. (2016). Global pharmaceutical regulation: the challenge of integration for developing states. *Globalization and Health*. doi:<https://doi.org/10.1186/s12992-016-0208-2>
- Pulla, P. (2022). India's speedy approvals of COVID-19 vaccines come under fire. *Science*, 442–443.
- RadioNew Zealand. (2021, March 6). *Vanuatu has two more Covid-19 cases in quarantine*. Retrieved from RadioNew Zealand: <https://www.rnz.co.nz/international/pacific-news/437807/vanuatu-has-two-more-covid-19-cases-in-quarantine>
- Regi, V. (2017). Medicines Regulatory Harmonization: international collaboration as a key to improve public health. *Med Access @ Point of Care*. Retrieved from <https://journals.sagepub.com/doi/pdf/10.5301/m.aapoc.00000001>
- Reuters. (2021, April 7). *Cambodia starts vaccinating textile factory workers*. Retrieved from Reuters: <https://www.reuters.com/article/us-health-coronavirus-cambodia-workers-idUSKBN2BU170>
- Reuters. (2020, June 06). *G20 pledges more than \$21 billion to fight coronavirus*. Retrieved from Reuters World News: <https://www.reuters.com/article/uk-health-coronavirus-g20-pledges-idUKKBN23D01U>
- Roth, L., Bempong, D., Babigumira, J. B., Banoo, S., Cooke, E., Jeffreys, D., ... Nwokike, J. (2018). Expanding global access to essential medicines: investment priorities for sustainably strengthening medical product regulatory systems. *Globalization and Health*. doi:<https://doi.org/10.1186/s12992-018-0421-2>
- Sauer, F. (2019). Pharmaceutical Harmonisation in Europe and Beyond. *Journal of Pharmacy and Drug Development*. Retrieved from <https://escientificpublishers.com/pharmaceutical-harmonisation-in-europe-and-beyond-JPDD-01-0010>
- Solis-Moreira, J. (2021, November 13). *How did we develop a COVID-19 vaccine so quickly?* Retrieved from Medical News Today: <https://www.medicalnewstoday.com/articles/how-did-we-develop-a-covid-19-vaccine-so-quickly>
- South-East Asia Regulatory Network (SEARN). (n.d.). *Action Point 5 – Strategy to Facilitate Reliance*. Retrieved from SEARN: <https://searn-network.org/action-point-5-strategy-to-facilitate-reliance>
- Strangio, S. (2021, September 08). *What Explains Cambodia's COVID-19 Vaccine Distribution Success?* Retrieved from The Diplomat: <https://thediplomat.com/2021/09/what-explains-cambodias-covid-19-vaccine-distribution-success/>
- Sujan, M. A. (2021, April 7). *South African variant of Covid-19 dominant in Dhaka: icddr,b study*. Retrieved from The Daily Star: <https://www.thedailystar.net/coronavirus-deadly-new-threat/news/south-african-variant-covid-19-dominant-bangladesh-icddr-b-study-2073757>
- Tan, J., Cook, M. J., Logan, P., Razanov, L., & Wilder-Smith, A. (2021). Singapore's Pandemic Preparedness: An Overview of the First Wave of COVID-19. *International Journal of Environmental Research and Public Health*. doi:<https://doi.org/10.3390/ijerph18010252>
- The College of Physicians of Philadelphia. (2018, January 17). *Vaccine Development, Testing, and Regulation*. Retrieved from The History of Vaccines: <https://www.historyofvaccines.org/content/articles/vaccine-development-testing-and-regulation>
- The Straights Times. (2020, March 23). *Australia starts lockdown measures as coronavirus cases jump*. Retrieved from The Straights Times: <https://www.straitstimes.com/asia/australianz/australia-starts-lockdown-measures-as-coronavirus-cases-jump>
- Thind, M., & Kowey, P. R. (2021). The Role of the Food and Drug Administration in Drug Development: On the Subject of Proarrhythmia Risk. *Journal of Innovations in Cardiac Rhythm Management*, 3958–3967.
- Tomić, S. (2011, June 15). *Accession Preparation: Situation in Croatia*. Retrieved from European Medicines Agency: https://www.ema.europa.eu/en/documents/presentation/presentation-accession-preparation-situation-croatia_en.pdf
- Tongia, A. (2018, January 29). *The Drug Regulatory Landscape in the ASEAN Region*. Retrieved from Regulatory Affairs Professionals Society: <https://www.raps.org/news-and-articles/news-articles/2018/1/the-drug-regulatory-landscape-in-the-asean-region>
- Tooze, A. (2021). *Shutdown: How Covid Shook the World's Economy*. New York (NY): Viking.
- United Nations Department of Global Communications (DGC). (2020, April 7). *UN mobilizes global cooperation in science-based COVID-19 responses*. Retrieved from United Nations COVID-19 Response: <https://www.un.org/en/un-coronavirus-communications-team/un-mobilizes-global-cooperation-science-based-covid-19-responses>
- United Nations Economic and Social Commission for Asia and the Pacific (UNESCAP). (2016). *Framework Agreement on Facilitation of Cross-border Paperless Trade in Asia and the Pacific*. Bangkok (TH): ESCAP.
- United Nations Economic and Social Commission for Asia and the Pacific (UNESCAP). (2020, May 20). *Socio-Economic Response to COVID-19: ESCAP Framework*. Retrieved from ESCAP: <https://www.unescap.org/resources/socio-economic-response-covid-19-es-cap-framework>

- Vietnam Investment Review. (2021, February 2). *COVID-19 vaccine AstraZeneca conditionally authorised for emergency use in Vietnam*. Retrieved from Vietnam Investment Review: <https://www.vir.com.vn/covid-19-vaccine-astazeneca-conditionally-authorized-for-emergency-use-in-vietnam-82469.html>
- Voysey, M., Costa-Clemens, S., & Mahdi, S. A. (2020). Safety and efficacy of the ChAdOx1nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *The Lancet*, 99–111.
- Wang, W., & Wertheimer, A. I. (2021). History, status and politicization of the FDA. *Research in Social and Administrative Pharmacy*. doi:<https://doi.org/10.1016/j.sapharm.2021.06.009>
- Wee, S.-L. (2018, November 11). In China, Desperate Patients Smuggle Drugs. Or Make Their Own. *New York Times*. Retrieved from <https://www.nytimes.com/2018/11/11/business/china-drugs-smuggled-homemade.html>
- Welfare, M. a. (2017, February 21). *WHO congratulates India on successful assessment of India's National Regulatory Authority*. Retrieved from Press Information Bureau: <https://pib.gov.in/newsite/PrintRelease.aspx?relid=158598>
- WHO and WTO Secretariat. (2004). *WTO Agreements and Public Health A Joint Study by the WHO and the WTO Secretariat*. Geneva (CH): WTO Secretariat.
- World Health Organization (WHO). (2021, April 14). *Technical Brief: Regulation of COVID-19 Vaccines Synopsis from the August 2020–February 2021 COVAX RAG meetings*. Retrieved from WHO: https://cdn.who.int/media/docs/default-source/medicines/regulatory-updates/covid-19/tech-brief_april-2021_regulation-of-covid-19-vaccines_synopsis_-_aug2020_feb2021.pdf?sfvrsn=93554ca9_7&download=true
- World Health Organization (WHO). (2021, December 23). *Achieving 70% COVID-19 Immunization Coverage by Mid-2022*. Retrieved from WHO: <https://www.who.int/news/item/23-12-2021-achieving-70-covid-19-immunization-coverage-by-mid-2022>
- World Health Organization (WHO). (2020, December 31). *WHO issues its first emergency use validation for a COVID-19 vaccine and emphasizes need for equitable global access*. Retrieved from WHO: <https://www.who.int/news/item/31-12-2020-who-issues-its-first-emergency-use-validation-for-a-covid-19-vaccine-and-emphasizes-need-for-equitable-global-access>
- World Health Organization (WHO). (2021). *Good Reliance Practices in the Regulation of Medical Products: High Level Principles and Considerations*. WHO Technical Report Series No. 1033, Annex 10. Geneva (CH): WHO. Retrieved from <https://www.who.int/publications/m/item/annex-10-trs-1033>
- World Health Organization (WHO). (2021). *Strategy to Achieve Global Covid-19 Vaccination by mid-2022*. Geneva (CH): WHO.
- World Health Organization (WHO). (2017). *Ten Years in Public Health, 2007–2017 – Report by Dr Margaret Chan, Director-General – Access to Medicines: Making Market Forces Serve the Poor*. Geneva (CH): WHO. Retrieved from <https://www.who.int/publications/10-year-review/chapter-medicines.pdf>
- World Health Organization (WHO). (2021). *WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report*. Geneva (CH): WHO.
- World Health Organization (WHO). (2021). *WHO Global Benchmarking Tool for Evaluation of National Regulatory System of Medical Products*. Geneva (CH): WHO.
- Xinhua. (2021, February 04). *Cambodia approves emergency use of China's Sinopharm COVID-19 vaccine*. Retrieved from Xinhua Net: http://www.xinhuanet.com/english/2021-02/04/c_139721602.htm
- Xinhuanet. (2021, June 15). *China's Sinopharm vaccine rolls out in Vanuatu*. Retrieved from Xinhuanet: http://www.xinhuanet.com/english/2021-06/15/c_1310008805.htm
- Yang, D. L. (2009). Regulatory learning and its discontents in China: Promise and tragedy at the State Food and Drug Administration. In J. Gillespie, & R. Peerenboom, *Regulation in Asia: Pushing Back on Globalization* (pp. 139–162). Oxford (UK): Routledge.
- Zhang, H., Guo, Z., & Shen, L. (2021). What Can We Learn from COVID-19 Drug Development and Access for Non-Pandemic Diseases? A Chinese Perspective. *The American Journal of Bioethics*, 42–45.
- Zheng, W., Yan, X., Zhao, Z., Yang, J., & Yu, H. (2021). COVID-19 vaccination program in the mainland of China: a subnational descriptive analysis on target population size and current progress. *Infectious Diseases of Poverty*. doi:<https://doi.org/10.1186/s40249-021-00909-1>

Further Reading

- World Health Organization (WHO), 2021; *Manual for benchmarking of the national regulatory system of medical products and formulation of institutional development plans*; available at: https://www.who.int/publications/m/item/Benchmarking_manual_V2_09Mar2021
- Organization for Economic Cooperation and Development (OECD), 2021, *Regulatory responses to the COVID-19 pandemic in Southeast Asia*, available at: <https://www.oecd.org/coronavirus/policy-responses/regulatory-responses-to-the-covid-19-pandemic-in-southeast-asia-b9587458/>
- Douglas Ball, Susan Roth, and Jane Parry, 2016; *Better Regulation of Medicines Means Stronger Regional Health Security*, ADB Briefs No. 54; available at: <https://www.adb.org/sites/default/files/publication/184392/better-regulation-medicine.pdf>
- National Academies of Science, Engineering and Medicine, 2020; *Regulating Medicines in a Globalized World: The need for increased reliance among regulators*; available at: <https://nap.nationalacademies.org/catalog/25594/regulating-medicines-in-a-globalized-world-the-need-for-increased>
- Uttara Soumyanarayanan, Mimi Choong, James Leong et al, 2021; *The COVID-19 crisis as an opportunity to strengthen global regulatory coordination for sustained enhanced access to diagnostics and therapeutics*, in: “Clinical and Translational Science”, Vol. 14.3, pp. 777–780 available at: <https://ascp.onlinelibrary.wiley.com/doi/10.1111/cts.12954>

Policies and Guidelines

- WHO, 2021; *Good regulatory practices in the regulation of medical products*, Annex 10 to the “WHO Expert Committee on Specifications for Pharmaceutical Preparations, Fifty-fifth report”; pp. 269 – 304; available at: <https://apps.who.int/iris/bitstream/handle/10665/340323/9789240020900-eng.pdf>
- WHO, 2021; *Good reliance practices in the regulation of medical products: high level principles and considerations*, Annex 10 to the “WHO Expert Committee on Specifications for Pharmaceutical Preparations, Fifty-fifth report”; pp. 237 – 264; available at: <https://apps.who.int/iris/bitstream/handle/10665/340323/9789240020900-eng.pdf>

WHO, 2021; COVID-19 Vaccines: Safety Surveillance Manual | Regulatory Reliance and Work-Sharing 2nd Edition, available at: <https://www.who.int/publications/i/item/9789240032781>

European Medicines Agency (EMA), 2019, *From laboratory to patient: the journey of a medicine assessed by EMA*; available at: https://www.ema.europa.eu/en/documents/other/laboratory-patient-journey-centrally-authorized-medicine_en.pdf

US Food and Drug Agency (FDA), *Guidance Document: Emergency Use Authorization for Vaccines to Prevent COVID-19*, available at: <https://www.fda.gov/media/142749/download>

Websites of Organizations Promoting Regulatory Cooperation

World Health Organization

COVID-19 vaccines technical documents: <https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials>

Capacity building and training materials:

<https://www.who.int/activities/capacity-building-and-training-materials>

COVAX:

<https://www.who.int/initiatives/act-accelerator/covax>

South-East Asia Regulatory Network (SEARN):

[https://www.who.int/southeastasia/activities/south-east-asia-regulatory-network-\(searn\)](https://www.who.int/southeastasia/activities/south-east-asia-regulatory-network-(searn))

Organization for Economic Cooperation and Development

Regulatory Policy and the COVID-19 Crisis <https://www.oecd.org/regreform/regulatory-policy/reg-covid-19-activities.htm>

Asia Pacific Economic Cooperation

Life Sciences Innovation Forum Regulatory Harmonization Steering Committee <https://www.apec.org/rhsc>

International Coalition of Medicines Regulatory Authorities (ICMRA) COVID-19 <https://www.icmra.info/drupal/en/covid-19>

Future Preparedness Regulatory and Policy Benchmarking Tool

A structured tool for policymakers: for each of five issues, the questions to ask, the challenges to expect and the measures to take.

ISSUE 1

01

Maintain Publicly Available and Up-to-date Lists of Approved Medicines

Guiding Question

1. Is it clear which domestic institution has the authority to do this, or put another way, has the NRA been explicitly vested with this authority?
2. Is this something the NRA already does in part (for newly approved medicines) or in full (for all medicines including those long on the market)?
3. If this is not done, what technical or resource constraints exist to establishing such a register?

Potential Challenges

In many developing countries a **lack of clear legislative or regulatory authority** to provide this and **severe resource constraints** may hinder the establishment and effective publication of such a list. Moreover, such a list must be published in such a way that is both easily accessible to the public and can be easily updated by the authorities, i.e., **in digital and online format**, which again raises questions of **resources and skills** to establish and maintain such a list.

Recommended Measures

1. As part of efforts to improve transparency around public health, and as part of broader digital transformation initiatives, governments should delegate the authority and allocate the necessary resources to the NRA to establish and maintain such a list.
2. 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 catalogue different medicines).

Mandate Time-Limits for NRAs to Adopt and Publish Regulatory Decisions

Guiding Question

1. How long does it currently take for the NRA to adopt and publish regulatory decisions in the context of approval procedures?
2. Is this in line with average timeframes for NRAs in countries at similar levels of economic development?
3. Did the COVID-19 pandemic result in the adoption and publication of regulatory decisions at a more expedited rate than has generally been the case prior to the pandemic?
4. What can the NRA do in future to permanently adopt some of the expedited decision-making that it resorted to in response to the COVID-19 pandemic?
5. What additional resources or authorizations would the NRA require in order to adopt such expediciencies?

Potential Challenges

For this particular recommendation, there must be both the **political will and the administrative capacity** to do a post-mortem of how the NRA expedited approvals during the COVID-19 pandemic and which innovations could be permanently adopted in future without compromising the NRA's core mission.

Recommended Measures

1. Carry out a study of time limits for the adoption and publication of regulatory decisions prior to and during the COVID-19 pandemic, identifying which innovations the NRA adopted to expedite the approval of COVID-19 vaccines.
2. Legislate the adoption of such innovations as can be permanently adopted without compromising the NRA's core mission, setting binding time limits for NRAs to adopt and publish regulatory decisions.
3. Allocate such resources as are necessary to support the NRA in the implementation of these new requirements.
4. Require the NRA to provide a semi-annual accounting of its success or failure in adhering to these new time-limits, with any failures being accompanied by reasons for their occurrence and internal recommendations for how such failures can be avoided in future.

Prescribe the Use of the WHO Collaborative Registration Process for Prequalified Products

Guiding Question

1. Is the NRA currently participating in the scheme?²⁶
2. If it is not participating, what are the main hurdles to participation?
3. Would there be considerable benefits to the main stakeholders of the country's public health sector (consumers, medical practitioners, hospitals, medical insurers) to joining the scheme?

Potential Challenges

The main obstacles to participation are likely to be either of a **political-economy nature** (i.e., existing market participants are more satisfied with the status quo), related to government concerns over a real or perceived **diminution in regulatory sovereignty** that joining the procedure may entail, or be due to **resource constraints**. In other cases, where regulatory capacity is already deemed sufficiently robust, this may seem unnecessary.

Recommended Measures (for those countries not participating in the WHO scheme)

1. Initiate a study on the costs/benefits of participating in the scheme and identify what the relevant constraints are.
2. If the government can demonstrate that the benefits outweigh the costs and can overcome any identified constraints, approach the WHO on joining the scheme.

ISSUE 4

Adopt Concrete Steps to Promote Cooperation between NRAs

04

Guiding Question

1. To what extent is cooperation between the country's NRA and more advanced NRAs already taking place either under regional cooperation arrangements or at the WHO?
2. Which NRAs in which countries would be the likeliest partners and would yield the best results in terms of different forms of cooperation over different time horizons?

Potential Challenges

This is primarily a matter of both **political will and sufficient resources**, with the primary constraint being the latter, particularly since the pandemic has markedly changed the political calculus as to the need to have robust regulatory capacity on hand.

Recommended Measures

1. Identify which forms of regulatory cooperation already exist with which foreign NRAs.
2. Identify those 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 happening.
3. Approach the governments of the foreign NRAs with which greater cooperation is sought and agree upon the terms and conditions subject to which such cooperation shall take place (MOU, MRA, etc.).
4. Allocate sufficient resources to the development and implementation of such regulatory cooperation initiatives.

ISSUE 5

Define and Implement a Dedicated Capacity Building Program for the NRA

05

Guiding Question

1. What is the most cost-effective and impactful way in which capacity can be built in the short to medium term?
2. Does this require large infusions of new resources and qualified staff? If so, how can such resources be secured (public budget and private sector contributions)?
3. Are short-term improvements to resourcing and staffing sustainable overtime to avoid “leakage” of any upgraded human capacity to the private sector?

Potential Challenges

This is first and foremost a **resource issue**, but also involves challenges of retaining any upgraded capacity over the medium to long term, which is a perennial problem for all capacity building efforts.

Recommended Measures

1. Identify which weaknesses in capacity are the most amenable to improvement over the short, medium and long terms.
2. Identify which avenues for capacity building are likely to be the most impactful and cost-effective (inhouse training, staff placements in foreign NRAs, secondments of staff from foreign NRAs, etc.).
3. Identify which foreign NRAs and other institutions can support the government in its efforts to upgrade the capacity of its own NRA, through institutional twinning programs and similar efforts.
4. If necessary, seek the help of capacity building experts in the field of regulatory approval of medicines at organizations like the WHO or stringent NRAs to support the government in drawing up and implementing its capacity building program.

NOTES

26 We note that some APAC NRAs are already participating in this scheme, such as Bangladesh, Bhutan, Laos, Malaysia, Philippines and Thailand; see: <https://extranet.who.int/pqweb/medicines/collaborative-registration-faster-registration>.



Country Case Studies

IN THIS SECTION

- 01 India
- 02 China
- 03 Singapore
- 04 Cambodia
- 05 Vietnam
- 06 Bangladesh
- 07 Vanuatu
- 08 Australia

How eight regional economies approved, procured and rolled out COVID-19 vaccines, and how their regulators cooperated with others.

COUNTRY CASE STUDY 1 OF 8

India



The NRA responsible for approval of COVID-19 vaccines in India is the Central Drugs Standard Control Organisation (CDSCO), under the oversight of the Directorate General for Health Services of the Ministry of Health and Family Welfare. The CDSCO is led by the Drugs Controller General of India (DCGI) – currently Dr. V. G. Somani – an official appointed by the central government. The DCGI is advised by the Drug Technical Advisory Board and the Drug Consultative Committee.

Through a sprawling organizational structure that includes offices and laboratories throughout the country and in major ports, the CDSCO approves new drugs but also performs a range of other regulatory functions. These include import registration and licensing, the licensing of inter alia, blood banks, vaccines and some medical devices and diagnostic agents, as well as representing India in WHO GMP schemes. It is also the CDSCO that approves testing protocols, carries out its own testing, publishes the Indian Pharmacopeia, and takes the lead on post-market surveillance for adverse drug reactions. Interestingly, it is not the CDSCO which is responsible for

pricing or even drug policy decisions, but rather the Ministry of Chemicals and Fertilizers by virtue of the National Pharmaceutical Pricing Authority (NPPA), which also maintains data on production, exports and imports, in addition to enforcing and monitoring the availability of medicines on the domestic market.

New drugs are only approved for marketing in India by the DCGI if they demonstrate that they are safe, effective and comply with Schedule Y of the Drugs and Cosmetics Rules (1945) made under the Drugs and Cosmetics Act (1940), which set out detailed guidelines and requirements for clinical trials (since 2019, these clinical trial requirements have been superseded by the New Drugs and Clinical Trials Rules). In 2006, a two-track system was introduced to expedite new drug approvals. For drugs which had already been approved by a stringent NRA (so-called “Category A” drugs), a fast-track approval procedure applies whereby drugs are approved for marketing in India within 2 to 4 weeks. For other (“Category B”) drugs, the deeper scrutiny required resulted in approval times of 12 weeks, once a complete application is submitted to the DCGI.

In 2017, an in-depth review (benchmarking) by the WHO of CDSCO found that the NRA had attained sufficient regulatory capacity to qualify it as a “functional” drug regulator, one classification below the maturity level required for an NRA to be considered a stringent regulator, and a distinction that only some 30 percent of NRAs in the world have earned. This positive assessment was critical for the country’s drug and vaccine industry, since it is a pre-requisite for WHO prequalification of vaccines.

For vaccines, the National Technical Advisory Group on Immunisation in India (NTAGI) was established in 2001 under the Department of Family Welfare within the Ministry of Health and Family Welfare, as part of broader efforts under the Universal Immunisation Program (UIP). A special working group on COVID-19 vaccines was established under NTAGI and first met in August 2020. The input of NTAGI in the approval process is only of an advisory nature, and the advice emanating from NTAGI has deviated at times from the decisions taken on approvals of COVID-19 vaccines by the CDSCO, for example in August 2021, when the NRA approved ZyCoV-D for use in both adults and adolescents.

India approved its first two vaccines on January 3rd, 2021, specifically a domestically produced version of the UK’s AstraZeneca vaccine, and the completely indigenous Covaxin, developed by Bharat Biotech. Approving the Indian vaccine proved controversial, given that at the time, its developer was still in the process of recruiting candidates for its Phase III trials.

Over the course of the vaccine rollout, as additional vaccines have been approved, there has been some criticism of the CDSCO as some have questioned its ability to stand up to political pressure.

From the outset, India’s efforts to develop and mass-produce vaccines was an effort steeped in international cooperation, not least because India’s pharmaceutical industry had undergone rapid transformation over the two preceding decades to position the country as the foremost vaccine supplier to the world. As early as March 2021, the majority of India’s vaccine manufacturers had signed exclusive licensing agreements with foreign partners for developing and manufacturing various COVID-19 vaccines, including with Oxford University and AstraZeneca for their vaccine, which was mass-produced in India and exported under the name Covishield, and the Russian-developed vaccine Sputnik V (approved by the DCGI in April 2021).

India’s vaccine diplomacy efforts saw the country take the lead in exporting vaccines to countries as far and wide as Afghanistan, Bahrain, Bangladesh, Bhutan, Fiji, Guatemala, Kenya, Maldives, Mauritius, Mongolia, Mozambique, Myanmar, Nepal, Nicaragua, Oman, Paraguay, Sri Lanka, and Uganda. India was also a major supplier to COVAX, although the country temporarily suspended exports in March 2021 as the Delta variant wave that swept the country in April and May 2021 began to take hold.

Sources: CDSCO website, Imran et al 2013, Pulla 2022, John 2010, Ministry of Health and Family Welfare 2017.

COUNTRY CASE STUDY 2 OF 8

China



The NRA responsible for approval of COVID-19 vaccines in China is the National Medical Products Administration (NMPA), which was established in its current form in 2013 through a restructuring of various different regulatory agencies. In 2018, it took on its current name and was merged into the newly created State Administration for Market Regulation, a kind of super-ministry responsible for the regulation of market competition, monopolies, intellectual prop-

erty, and drug safety, directly under the State Council of the People’s Republic of China.

The NMPA’s powers are wide-ranging and include drafting and implementing policy, legislation and regulation on food, drugs (including traditional Chinese medicines), medical devices and cosmetics. The NMPA also publishes the national pharmacopeia and is responsible for the registration (approval) and post-marketing surveillance of drugs and medical devices.

According to a 2018 New York Times' report, in the first decade and a half of the new millennium, just over 100 new drugs were approved in China, which is about one-third the number that had been approved in developed countries, with approvals typically taking seven to eight years. However, this finding is contradicted by academic research undertaken by Dali Yang, who notes that in 2006 alone, the Chinese food and drug regulator approved 1803 new drugs, although some of these approvals had to be withdrawn subsequently for lack of regulatory stringency.

China's regulatory framework for medicines was assessed by the WHO under the organization's Benchmarking Toolkit in 2011 and 2014, after which, like India in 2017 (discussed above) it was recognized as a functional regulatory agency, thereby laying the foundation for WHO prequalification of Chinese vaccines.

After early stumbles surrounding how to deal with the initial outbreak in Wuhan, the central government leadership in Beijing moved quickly once the scale of the threat posed by COVID-19 became apparent. In responding to the new virus in the early months of 2020, the Chinese authorities approved large funding allocations for research and development, as well as pooling resources from various research institutions to focus on several areas, including new medicines and vaccines, of which potential candidates were identified across various categories, including inactivated vaccines, recombinant protein vaccines, live attenuated influenza vaccines, adenovirus vaccines, and nucleic acid-based vaccines. For its part, the NMPA wasted no time in reviewing applications for the approval of emergency medical treatments.

As a result of these efforts, by both authorities and the community of epidemiology researchers, China was able to identify and genetically map the novel coronavirus by 9 January 2020. By the end of the same month, the NMPA had approved four diagnostic

kits for the virus, and by the end of May 2020, it had authorized 19 applications for clinical trials for medicines and vaccines to both prevent infection and treat infected patients.

By July 2020, China had begun authorizing the emergency use of vaccine candidates for high-risk groups, including Sinovac's vaccine (also known as CoronaVac), making China one of the first countries to approve a COVID-19 vaccine candidate.

By its very nature, the Chinese efforts to develop and test different vaccine candidates relied to a high degree on international regulatory cooperation, since China's initial success in combatting the virus meant there were simply not enough patients for domestic phase III trials to be conducted within China. Instead, these trials were conducted in countries where the virus was both rampant and governments were eager to get their hands on any vaccine that they could obtain. These two preconditions prevailed in a number of large and populous countries, including Indonesia, Turkey and Brazil. Indeed, it was thanks to results from phase III trials conducted in these three countries that in February 2021, the NMPA approved a second Chinese vaccine (Sinovac) for general public use.

China also engaged in a huge vaccine diplomacy effort, sending mostly commercial exports of vaccines to countries in South-East Asia, Africa and Latin America (where it became the main supplier), as well as to Hungary, the only EU country that included Chinese vaccines in its domestic vaccination campaign.

By June 2021, the NMPA had granted conditional market or emergency use authorization to a total of seven domestically produced vaccines, two of which had also been listed by the WHO for emergency use.

Sources: Wee 2018, Yang 2009, Zhang et al 2021, Nolte 2022.

COUNTRY CASE STUDY 3 OF 8

Singapore



The NRA responsible for approving COVID-19 vaccines and treatments in Singapore is the Health Sciences Authority (HSA), a statutory board under the

Ministry of Health of the Government of Singapore. The HSA is a stringent regulator, that in February 2022 was assessed using the WHO Global Bench-

marking Tool and was subsequently hailed as the world's first to achieve the highest maturity level in WHO classification (ML4) of regulatory authorities for medical products.

The HSA, which since 2019 is no longer responsible for food safety, has three functions under the governing legislation currently in force (the Health Products Act 2007), being the national regulator for health products, securing the national blood supply, and providing national expertise in forensic medicine, forensic science, and analytical chemistry testing capacities. It is in executing this first function that the HSA evaluates product approval applications, oversees and assesses clinical drug trials, as well as auditing good manufacturing practices and conducting post-market surveillance of health products marketed in Singapore.

Through various memoranda of understanding, Singapore has formalized close working relationships with NRAs in other countries, including other stringent regulators such as the US FDA, Health Canada, Swissmedic, the Australian Therapeutic Goods Administration and with less mature NRAs such as China's National Medical Products Administration (NMPA). The HSA also cooperates extensively with its counterparts in ASEAN member states thanks to long ongoing regulatory cooperation efforts in ASEAN, as discussed in the text of this paper (Section 5.2).

Particularly through its involvement in the ACCESS Consortium, comprising stringent NRAs from Australia, Canada, Singapore, Switzerland and the United Kingdom, Singapore's HSA worked on the articulation and dissemination of technical guidance on a range of issues, including the regulatory evidence requirements for COVID-19 vaccine approvals and considerations for post-market pharmacovigilance and later on COVID-19 medicines.

Singapore was the first country in Asia to approve the Pfizer-BioNTech's coronavirus vaccine for emergency use (known in Singapore as interim authorization)

on 14 December 2020, just 3 days after the USFDA had done the same. The Singaporean government had been at the forefront of efforts to support promising vaccine candidates and secure vaccine supplies, investing heavily to sign advanced purchase agreements and make advance down payments to candidates in both the United States and China, including Pfizer BioNTech, Moderna and CoronaVac.

In August 2021, the Singaporean Ministry of Health announced that it would recognize all COVID-19 vaccines accepted on the WHO Emergency Use Listing (EUL) and by extension would confer fully vaccinated status to anyone who could demonstrate having been inoculated with a vaccine on the WHO EUL.

It was Singaporean Prime Minister Lee Hsien Loong who is generally credited with coining the phrase "vaccine multilateralism" at the Global Vaccine Summit which took place in June 2020, offering whatever support the small nation state could provide in shaping the conversation around ensuring equitable access to COVID-19 vaccines. Singapore was also an early supporter of the COVAX Facility, and launched – together with Switzerland – the informal grouping known as the Friends of COVAX Facility (FOF) to catalyse discussions about the COVAX Facility and generate a significant body of support among self-financing countries to support efforts at achieving vaccine equity.

Given its overriding economic dependence on international travel and trade, Singapore consistently took the lead in efforts to restore normality, from becoming, in August 2021, one of the first countries to fully vaccinate 80 percent of its population, to reopening its land border with Malaysia at the end of November 2021 after each country agreed to mutually recognize the other's vaccine certificates, to being one of the first countries to officially abandon a zero covid strategy in favour of one entitled "living with covid".

Sources: HSA 2020, Bhatia 2020, Ministry of Health Singapore 2021, Fortune 2021.

COUNTRY CASE STUDY 4 OF 8

Cambodia



The national medical regulatory authority in Cambodia is the Department of Drugs and Food (DDF) under the Ministry of Health (MOH), established by virtue of the 1996 Law on the Management of Pharmaceuticals. In its capacity as NRA, the DDF regulates the market for a range of products and devices, including pharmaceuticals, traditional medicines, health supplements, food, medical devices, and cosmetics, with the power to approve or reject applications for marketing authorization, and conduct post marketing surveillance and enforcement.

Although clinical trials are possible in Cambodia in theory, with the National Ethics Committee (NEC) of the National Institute of Public Health under the MOH having statutory authority to govern and regulate such trials, in practice, the NEC has never authorized any request to conduct clinical trials beyond basic questionnaire-based studies that do not involve the introduction of new or novel pharmaceuticals or medical treatments.

Given its status as an ASEAN Member State, Cambodia has enacted the ASEAN Common Technical Requirements (ACTR) and ASEAN Common Technical Dossier (ACTD), which together essentially outline the procedures and protocols subject to which pharmaceutical products must be manufactured, registered and maintained in the regional group.

A Chinese media report dated February 4, 2021 announced the recent emergency use approval, by the Cambodian health authorities, of the Sinopharm vaccine, of which a significant number of doses would ultimately be provided to Cambodia as part of its highly successful national vaccination campaign. This was followed, on 22 February, by emergency use approval of the AstraZeneca vaccine by the Cambodian health authorities, approximately a week after it had been

listed by the WHO for emergency use, with the first 300,000 doses of the UK-developed vaccine being delivered on 2 March 2021.

An October 2021 report lists some 20 vaccines all approved for emergency use in Cambodia, including the Russian Sputnik vaccine, the US Pfizer and Moderna vaccines, France's Sanofi vaccine and Cuba's Soberana vaccines, as well as various Indian-developed vaccines.

Of the just-over 30 million doses that Cambodia received to inoculate its roughly 16 million population, 27 million doses were of Chinese vaccines, which shows the country's leadership prioritized the rapid execution of its national vaccination campaign by any means over any other considerations. This strategy ultimately proved successful so that Cambodia was able to boast vaccination rates on par with its much wealthier regional counterpart Singapore, as well as open up its economy at roughly the same time as the advanced city state and thus many months ahead of its ASEAN peers.

An August 2021 report noted that “the best vaccine is the one you can get” and that Cambodia was using a mix of Western and Chinese non-mRNA vaccines, including Sinovac, Sinopharm, AstraZeneca and Johnson & Johnson. The same report credits innovations in Cambodia's distribution strategy for its success, noting that a “clear and simple ring-fenced distribution plan based on location” rather than more complex to administer age (or risk) tiering allowed Cambodia's vaccination campaign to proceed swiftly, as did the use of the military to support distribution and delivery.

Sources: Khmer Times (2021), McGinley and Higgins (2021), Strangio (2021), Xinhua (2021)

COUNTRY CASE STUDY 5 OF 8

Vietnam



The Drug Administration of Vietnam (DAV) is the NRA responsible for the approval and post-market surveillance of drugs, biologics, vaccines and cosmetics and operates under the authority of the Ministry of Health.

Similar to other NRAs in the region, Vietnam is active in ASEAN-wide efforts to align regulatory procedures and protocols and uses the ASEAN Common Technical Dossier (ACTD) for approvals and also has a history of relying on previous guidance issued by stringent

regulatory authorities, such as the US FDA and the Japanese Pharmaceuticals and Medical Devices Agency (PMDA).

The Vietnamese NRA has performed well in WHO benchmarking reviews of its regulatory capacity. In April 2015 it achieved “Functional” status when audited against the WHO’s Vaccine Assessment Tool. Then, following another review in 2018 which further helped the Vietnamese NRA to strengthen its capacity, in 2021 the WHO announced that the DAV had achieved Maturity Level 3, the second highest in the WHO classification of national regulatory systems.

The Vietnamese health authorities were relatively quick to grant emergency use approval to the Oxford-AstraZeneca vaccine, doing so at the end of January 2021 (with the formal decision signed on 1 February), followed by Sputnik V on 23 March. Further approvals followed in June, first for Sinopharm then for the Pfizer-BioNTech and then the Moderna vaccines, with the Johnson & Johnson vaccine being approved the following month on 15 July. These approvals were then followed later in the year with further emergency use approvals for the Cuban Abdala and the Indian Covaxin candidates in September and November 2021 respectively.

Despite initial successes in managing the pandemic in 2020, Vietnam’s vaccination program was slow to

pick up momentum, leaving the country exposed to the Delta variant which arrived in the spring of 2021 and began wreaking havoc by the 2nd and 3rd quarters of the year, with the larger urban centers in oppressive lockdowns which tested the peoples’ faith and trust in the government’s ability to successfully manage the pandemic.

The government of Vietnam is reported to have placed early orders for the Russian Sputnik V vaccine in August 2020, but effectively began its vaccination campaign – albeit haltingly – only in the second week of March 2021, with a relatively small initial delivery of some 117,600 doses of the AstraZeneca vaccine. Over the course of 2021, and as the country continued to wage a tough battle with the pandemic, donations poured in from across the region and the world, including from the United States, China, Japan, Australia and Italy.

At the time of writing (June 2022), Vietnam, which has vaccinated over 80 percent of its population, has relied predominantly on mRNA vaccines from Pfizer and Moderna, which account for roughly half of all doses administered, with AstraZeneca and Sinopharm making up most of the remainder.

Sources: Nikkei Asia (2021), Vietnam Investment Review (2021), Clark (2021).

COUNTRY CASE STUDY 6 OF 8

Bangladesh



The Directorate General of Drug Administration (DGDA) is the NRA in Bangladesh responsible for the approval of medicines, including vaccines. The DGDA has regulatory oversight and the ultimate responsibility for implementing the prevailing laws and regulatory frameworks relating to the importation and procurement of both inputs and packaging for pharmaceutical products, as well as the manufacture and import of finished medicinal products, their export, domestic marketing and pricing.

The 2016 Drug Policy recognizes the importance of upgrading the NRA, and explicitly lists this as a priority objective as well as articulating various pathways by

which this is to be accomplished, including, appointing professionally qualified and experienced human resources, providing regular training to personnel working in the areas of drug approvals, and the regulation of manufacturing, storage, distribution, sale, import, export and quality control. The 2016 Drug Policy also calls for the human resource development plan, together with the adoption of a career development plan and an internal promotion system based on entirely objective and meritocratic metrics. The explicit goal mentioned here is accreditation with the WHO and membership of the PIC/S.

The DGDA announced emergency use approval for the AstraZeneca vaccine on 5 January 2021, with plans to procure the majority of the country's inoculation needs from the Serum Institute of India. However, when India imposed an export ban on vaccines in March and April of 2021 due to a domestic surge in cases, Bangladesh was forced to begin approving and importing other vaccines, starting first with the Russian Sputnik V vaccine, which was approved on April 27, followed shortly thereafter by China's Sinopharm two days later. By October 2021, Bangladesh had approved 7 vaccines. A domestic candidate, Bangavax developed by Globe Biotech Ltd. was reported to be in clinical trials in Bangladesh, with an approval decision pending the outcome of these trials, but as of the current writing remains unapproved by the DGDA.

As vaccine supplies dried up from India in early 2021, donations from other countries started to pour in, including from the United States, which by February 2022 was the largest single donor to the country, having donated over 61 million doses of the Pfizer and Moderna vaccines. Other countries that donated vaccines to Bangladesh include Japan (AstraZeneca) and China (Sinopharm). Indeed, the DGDA appeared to be tailoring approvals in order to meet announced or incoming vaccine shipments, as it did when it approved the Moderna vaccine on 29 June 2021, four days after an announcement that it would receive some 2.5 mil-

lion doses of the vaccine from COVAX in the next 10 days.

The development of the domestic pharmaceutical industry in Bangladesh has enjoyed significant support from the WHO. In 2016, a coalition of interested partners was established to support efforts by local manufacturers to meet the requirements of the WHO Prequalification of Medicines Program (PQP). This coalition, worked to coordinate the efforts of development partners, and with technical backstopping from WHO, and under the leadership of DGDA was able to support the country in building local capacity to manufacture and regulate medicines, so that a first PQP approval could be granted in 2019 to Beximco Pharmaceuticals. WHO and DGDA staff conducted GMP inspections together, which again helped strengthen the capacity of the DGDA.

The DGDA has also partnered with the WHO in the context of the organization's Benchmarking Tool, with an interim assessment being conducted in September 2018, which resulted in an institutional development plan being adopted as a roadmap for supporting the DGDA in its efforts to obtain maturity level three, which USAID has also been supporting with training and technical assistance.

Sources: DGDA (2022), Paul (2021), Dhaka Tribune (2021), WHO (2019).

COUNTRY CASE STUDY 7 OF 8

Vanuatu



The Ministry of Health is the organization tasked with the small island nation's vaccine rollout, and does not appear to possess the regulatory capacity to carry out independent approvals of medicines and vaccines. Instead, Vanuatu works closely with the World Health Organization and relies on the WHO's Model List of Essential Medicines.

The first National Medicines Policy for Vanuatu was enacted in 2015 and identifies some eight key objectives, including improvement of medicines regulation and quality. The policy lists as an aspirational goal, that "medicines to be used in the Republic of Vanuatu (both public and private) should be registered for use."

By the same token, the 2015 Policy also articulates the aspiration that "applicable legislation to regulate the manufacture, importation, exportation, marketing, distribution, prescribing and dispensing and use of medicines will be formulated and implemented". The 2015 Policy commits to working towards these goals, without specifying a timeframe for doing so.

The WHO Country Cooperation Strategy (2018-2022) for Vanuatu lists a number of strategic priorities aimed at improving the regulatory capacity responsible for overseeing and managing the health care system, including to "review, revise and update the health sector policy framework" and "review, develop

and update legislation, policies and guidelines in accordance with International Health Regulations (2005).

In terms of the authorities' efforts to vaccinate the population, only two vaccines have been approved for use in Vanuatu, namely AstraZeneca and Sinopharm. This decision was heavily motivated by the ease of storage and distribution of these particular vaccines, compared to the extensive cold-chain requirements of mRNA vaccines such as Pfizer and Moderna, which are virtually impossible to meet under current conditions in the Western Pacific.

The original planning by Ministry of Health officials released in early 2021 envisaged a slow campaign beginning in April and which would only be complete in 2023 – a relaxed timeline compared with the efforts of

many other countries to vaccinate as much of their population as quickly as possible. As it turned out, the campaign was only launched in June of 2021. Reports differ as to current vaccination rate. Reporting by the authorities dated May 2022 indicate that some 75 percent of the population on average had received 2 doses and was thus fully vaccinated. According to these reports, some islands and areas enjoy higher vaccination rates than others, with Port Vila, the capital, boasting a vaccination rate of 92 percent fully vaccinated, while at the other extreme, Tafea is still languishing below 50%. These numbers stand in stark contrast to data published by other sources, with Our World in Data reporting as of 25 April 2022, a vaccination rate of only 38.5 percent.

Sources: Ministry of Health of Vanuatu, WHO, Xinhuanet (2021), McGarry (2021).

COUNTRY CASE STUDY 8 OF 8

Australia



The Therapeutic Goods Administration (TGA) is the NRA charged with approving medicines (including vaccines) and which took the lead during the COVID-19 pandemic for approvals of various vaccine candidates. Operating under the Australian Department of Health, the TGA regulates the quality, supply and advertising of medicines, pathology devices, medical devices, blood products and most other therapeutics.

The TGA is a stringent regulatory authority that works together with other similarly mature NRAs in the framework of the Access Consortium, comprising (in addition to the TGA), the NRAs from Canada, Singapore, Switzerland and the United Kingdom. Working together through the Consortium, the participating NRAs have successfully completed joint reviews of both innovative and generic medicines and are reported to have received a significant number of expressions of interest from sponsors intending to file through the Consortium's collaborative pathway.

TGA participates in other international collaborative initiatives in addition to the Access Consortium, including International Coalition of Medicines Regulatory Authorities (ICMRA), International Medical Device Regulators Forum (IMDRF), the International

Over-The-Counter (OTC) Medicines Regulators Forum, the International Pharmaceutical Regulators Programme (IPRP), and Project Orbis, an initiative led by the US FDA to provide patients access to promising new cancer treatments.

The TGA is also an important collaborative partner in the region, given its status as a stringent NRA, an example of which is the Pacific Medicines Testing Program which was launched in 2017 to enhance regional health security. By virtue of this program, the TGA, working with other partners, is piloting a program to provide Pacific Island countries access to Australian laboratory testing for medicines quality assurance undertaken by the TGA's Laboratories Branch. The TGA laboratories have also been designated by the WHO as both a WHO Collaborating Centre for Drug Quality Assurance and a WHO Collaborating Centre for Quality Assurance of Vaccines and other Biologicals.

At the time of writing, the TGA has approved five vaccines for use in the Australian vaccination campaign, which began in February 2021. The Pfizer–BioNTech vaccine was approved on 25 January 2021, with approval of the Oxford–AstraZeneca vaccine following in mid-February. Johnson & Johnson's Janssen vaccine

was approved on 25 June 2021 (but is not included in the nationwide vaccination program), and the Moderna vaccine was approved on 9 August 2021, followed by the provisional approval of the Novavax vaccine in January 2022.

For the purposes of travel to Australia, the Australian Government recognizes – as per January 2022 – a number of additional vaccines not included in the national vaccination rollout, namely the Chinese vaccines by Sinovac and Sinopharm, the Indian vaccine developed by Bharat Biotech and the Russian Sputnik V vaccine.

Despite what was an initially slow rollout, with Australia languishing at the bottom of the OECD in terms of vaccination rates until the third quarter of 2021, the onslaught of the Delta variant caused the eastern seaboard States of New South Wales and Victoria to abandon their hitherto Covid-zero policies and embark on a race to vaccination, which was also joined by all other States, with various degrees of urgency. At the time of writing, Australia enjoys vaccination rates in excess of 90 percent.

Sources: TGA website, Australian Government Department of Health (2021).