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PERSPECTIVE

RESEARCHERS AT ISEAS – YUSOF ISHAK INSTITUTE ANALYSE CURRENT EVENTS

Singapore | 23 February 2023

The Vaccine R&D System and Production Network in Thailand: Possibilities for Strengthening Domestic and International Partnerships

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People wait to receive doses of Pfizer, AstraZeneca/Oxford and Sinovac Covid-19 coronavirus vaccine booster shots inside a stadium in Bangkok on 8 January 2022. Picture: Lillian SUWANRUMPHA/AFP.

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EXECUTIVE SUMMARY

- While Thailand enjoys self-sufficiency in many of the vaccines it needs, when COVID-19 hit, the country's R&D preparedness and response were not strong enough to develop vaccines in a timely manner. And amid supply shortages after COVID-19 vaccines were developed, Thailand, like the rest of ASEAN, initially relied on vaccines produced elsewhere.
- Thailand ranks high among ASEAN countries in many indicators of R&D inputs and outputs. However, its R&D and innovation systems are not yet sufficiently developed to translate vaccine R&D inputs into patents that can then lead to new vaccines.
- Public and private pharmaceutical firms in Thailand conduct vaccine R&D in the national immunisation programme in collaboration with universities and research institutes in Thailand and abroad. Thailand is also home to many international and domestic contract research organisations.
- ASEAN has launched several initiatives to strengthen its biomedical R&D infrastructure and human resources, build a network of research centres across the region, and promote cooperation in R&D among ASEAN members, ASEAN's Dialogue Partners, the United States, and the European Union.
- Thailand and ASEAN can strengthen their vaccine security by pooling and coordinating their financial and scientific resources to address diseases of regional concern.

INTRODUCTION

Although non-communicable diseases are now the main drivers of mortality and morbidity rates in Thailand, some infectious diseases still have high levels of incidence and prevalence.¹ In most circumstances, particularly when no therapeutic drugs are available and in low-income settings, vaccines are a cost-effective public health intervention in controlling the spread of, and reducing mortality and morbidity from infectious diseases.²

Thailand not only self-procures many of the vaccines in its Expanded Programme on Immunisation, but it is also ASEAN's second-largest vaccine exporter after Indonesia, mainly of influenza vaccines to other ASEAN countries.³ Still, in 2020, Thailand reported more than 60,000 cases of vaccine-preventable diseases.⁴

KEY INDICATORS IN THE THAI BIOMEDICAL AND VACCINE R&D SYSTEM

Developing effective vaccines rapidly requires strong vaccine research and development (R&D) preparedness and response. As illustrated by the rapid development of vaccines for COVID-19, R&D preparedness and response necessitates not only adequate financial and scientific resources, but also a policy and regulatory R&D environment that fosters innovation, public-private partnerships, and international cooperation.

Vaccine R&D is also essential for achieving the UN's Sustainable Development Goal 3 (SDG 3: Ensure healthy lives and promote well-being for all ages), and other SDGs that depend on healthy people and populations.⁵ In fact, some SDG targets include indicators related to biomedical R&D.

The diversity in economic development within ASEAN is mirrored by variability in terms of R&D intensity. Thailand ranks among the ASEAN countries with higher inputs and outputs indicators in biomedical R&D. In 2017, gross expenditures on R&D relative to GDP (SDG indicator 3.b.2) in Thailand stood at 1.0%, only behind Singapore (1.9%) and Malaysia (1.4%).⁶ In countries with total R&D spending above 1%, the private sector tends to be a major, often the largest, contributor to R&D expenditures (Table 1). The private sector accounts for 80.8% of total R&D expenditures in Thailand, the largest in ASEAN. In 2018, Thailand had 1,350 researchers per million inhabitants in full-time equivalents (SDG indicator 9.5.2), the third largest in ASEAN.

Table 1				
R&D Inputs Indicators	Thailand	Singapore	Malaysia	Indonesia
Total R&D expenditures (% of GDP) (2017)	1.00	1.92	1.04	0.22
Government R&D expenditures (% of GDP)(2017)	0.05	0.21	0.14	0.16
Business Enterprise R&D expenditures (% of GDP) (2017)	0.80	1.15	0.46	0.02
Private Non-profit R&D expenditures (% of GDP) (2017)	0.80	N/A	N/A	0.01
Researchers per million inhabitants in full time equivalents (2018)	1350.3	6802.5	2184.7	216

Source: Endnote 6

Regarding R&D output indicators, the picture is mixed (Table 2). On the one hand, Thai researchers are among the most productive in ASEAN in terms of the number of academic publications and clinical trials, but they lag in the number of patents. Thailand trails Indonesia, Malaysia, and Singapore in the number of articles published in peer-reviewed journals in the broad field of biomedicine, but when it comes to the specific topic of vaccines, Thai researchers published more articles than their peers elsewhere in ASEAN countries, and were only behind China, Japan, India, the Republic of Korea and Iran in all of Asia.⁷

A bibliometric analysis of the articles published in 2019 by ASEAN scientists indicates that Thai researchers collaborate more with scientists from the United States and Australia than with colleagues from other ASEAN countries.⁸ The Southeast Asian office of the WHO established as one of the objectives of its *2016-2020 Vaccine Strategic Plan* the participation of all countries in vaccine clinical trials.⁹ As of March 2022, the Asia-Pacific region had conducted 24.1% of all vaccine clinical trials in the world, led by China with 571 trials. Thailand, with 200 vaccine clinical trials, ranked first in ASEAN (36.5% of all vaccine clinical trials in ASEAN) and fourth in Asia Pacific.¹⁰

However, research does not necessarily generate economic value if it does not create new products, services, and/or processes. Thailand has still to translate its investments, publications, and clinical trials into patents, which is a good proxy of a country's ability to innovate. As of March 2022, Thailand had 41 patents in the field of biotechnology and 47 in pharmaceuticals, 7 times fewer than Malaysia and 20 times fewer than Singapore.¹¹

Table 2				
R&D Output Indicators	Thailand	Singapore	Malaysia	Indonesia
Scientific journal publications on vaccines (March 2022)	2819	1967	1456	636
Number of vaccine clinical trials (March 2022)	200	75	27	41
Share of Asia Pacific vaccine clinical trials (%) (March 2022)	7.6	2.9	1	1.6
Share of world's vaccine clinical trials (%) (March 2022)	1.8	0.7	0.2	0.4
Number of patents granted in biotechnology (March 2022)	41	752	278	2
Number of patents granted in pharmaceuticals (March 2022)	47	757	280	29

Source: Endnotes 7, 10, 11

MAIN PLAYERS IN THE THAI VACCINE R&D SYSTEM

As in other middle-income Asian economies, vaccine R&D and production in Thailand is centred on traditional technology vaccines included in its Expanded Programme on Immunisation. Thai vaccine manufacturers do not yet have the technological capacity to produce mRNA vaccines. As the R&D and production capabilities of Thai and ASEAN vaccine manufacturers improved, many of their vaccines had been exported to developing countries within Asia and beyond.

The policy process and government agencies involved in establishing vaccine security policy, deciding which vaccines should be included in the National List of Essential Vaccines as well as creating the regulatory framework for licensing and marketing of vaccines have been described in detail elsewhere.¹² The main government agencies that participate in setting the R&D agenda and allocating research funds are the *Thai National Institute of Health* (TNIH), Department of Medical Sciences, Ministry of Public Health, MoPH), the *National Research Council of Thailand*, the *National Science and Technology Development* (NSTDA), the *National Science Technology and Innovation Policy Office*, and the *Thailand Centre of Excellence for Life Sciences*. The TNIH is one of only five Asia Pacific R&D funding organisations included in the Global Research Collaboration for Infectious Disease Preparedness (GLOPID-R), an international coalition of funders of R&D to combat infectious diseases with pandemic potential. Regarding vaccine R&D, various organisations within the MoPH regulate and fund early preclinical research stages; namely, the *Food and Drug Administration*, the *National Vaccine Institute* (NVI), and the *Department of Disease Control*. Among its institutional goals, the NVI aims to strengthen R&D infrastructure, including training and capacity building, and technology transfer through its training vaccine centre.

The main pharmaceutical firms involved in vaccine R&D and manufacturing are the state-owned Government Pharmaceutical Organisation (GPO), the Queen Saovabha Memorial Institute-Thai Red Cross (QSMI), and the private firm BioNet Asia. The GPO conducts vaccine R&D and accounts for a significant share of Thai vaccine manufacturing, and it also exports vaccines to other ASEAN countries.¹³ The QSMI packages and distributes serums and rabies vaccines. Both companies are members of the Developing Countries Vaccine Manufacturers Network (DCVMN), which encompasses 41 public and private pharmaceutical firms in developing countries.¹⁴ BioNet Asia is one of the most active and innovative ASEAN firms, and the only Thai firm that produces vaccines prequalified by the WHO for procurement by UN agencies and governments.¹⁵ Bionet has developed low-cost vaccines for Haemophilus influenzae type b (Hib) using traditional technologies and, in collaboration with the NSTDA and several Thai research institutes, has patented processes for the development of a dengue vaccine.

Several Thai public and private pharmaceutical firms and universities have engaged in collaboration with foreign organisations for R&D and production of vaccines. For instance, BioNet has developed a pentavalent vaccine covering diphtheria, tetanus, pertussis, hepatitis B, and meningitis in collaboration with the Thai NSTDA and with South African scientists.¹⁶ Bionet also partnered with the NSTDA and Mahidol and Chiang Mai universities, to develop a dengue vaccine, which was later improved through a partnership with the Sanofi Pasteur Institute and the biotech firm In-Cell-Art in France. Sanofi Pasteur has also established a joint venture with the GPO (GPO-Merieux Biological Products, GPO-MBP) to conduct process development and finish-and-fill for new vaccines for ASEAN countries. Under the arrangement, Sanofi Pasteur supplies the vaccine in bulk and the GPO-MBP formulates and releases finished forms. The *Thai Armed Forces Research Institute of Medical Sciences* also conducts R&D on vaccines for enteric diseases, malaria, and HIV-AIDS. The MoPH has partnered with the USA's NIH and the United States Military HIV Research Program to conduct clinical trials for an HIV vaccine. And Siam Bioscience was selected by Astra-Zeneca to produce its COVID-19 vaccine for ASEAN countries, and obtained the WHO's approval.

Although the development of vaccines using the newest mRNA technologies still remains concentrated in a handful of American and European companies (Moderna, Pfizer/BioNTech, Curevac), some of them have plans to open manufacturing plants in developing countries.¹⁷ In Thailand, the *Chula Vaccine Research Centre* at Chulalongkorn University and the King Chulalongkorn Memorial Hospital have joined forces with BioNet to develop and manufacture the first Thai-made mRNA vaccine for COVID-19, the ChulaCov19 BNA159 vaccine. Stages 1 and 2 of clinical trials for this vaccine have been conducted in Australia.¹⁸

The offshoring by global pharmaceutical firms of R&D activities to developing countries can potentially lead to technology transfer and enhance the R&D and manufacturing capabilities of domestic biotechnology firms. Many of the global pharmaceutical firms with a presence in Thailand conduct late manufacturing stages for vaccines and therapeutic drugs. However, they have chosen other Asian countries (mainly China, India, Japan, the Republic of Korea, and Singapore) in which to establish regional R&D centres. Many of these global pharmaceutical firms have outsourced some of their R&D, initial clinical trials but increasingly other tasks as well (preclinical research, applications for ethical committees, and regulatory authorities) to so-called contract research organisations (CROs). Thailand is home to several of the largest

global CROs (Covance, ICON, IQVIA, Novotech, Parexel, PPD, Synchron, and Syneos Health) but also to local firms such as Aclires and Asia Global Research.¹⁹

VACCINE R&D COOPERATION IN ASEAN AND BEYOND

The COVID-19 pandemic has shown how international cooperation can accelerate vaccine development. It has also exposed how beggar-thy-neighbour policies, such as export restrictions on medical protective equipment and vaccine nationalism, can leave many developing countries at the expense of donor countries to secure vaccines for their most vulnerable populations.²⁰

In the context of a pandemic, vaccine production may not be sufficiently elastic, opening the debate about whether or not countries should strengthen their vaccine security by developing their vaccine R&D and manufacturing capacity. Most developing countries lack the financial and technological resources to invest in vaccine R&D. In addition, it is not sensible to replicate R&D capabilities in each country. Instead, international agreements to facilitate unimpeded trade and global/regional cooperation should ensure vaccines for countries without R&D and vaccine production capabilities.

During the 2003-2004 SARS epidemic, the ASEAN Secretariat issued recommendations to contain the epidemic.²¹ ASEAN has also been very active during the COVID-19 pandemic with multiple initiatives, including the establishment of the *ASEAN Centre for Public Health Emergencies and Emerging Diseases*, and the *ASEAN Public Health Emergency Coordination System* programme to coordinate national and regional preparedness and response to health emergencies. The *ASEAN Committee on Science and Technology* (COST), a committee to promote cooperation in science, technology, and innovation (ST&I) among ASEAN members, formulated the *2016-2025 ASEAN Plan of Action on ST&I* (APASTI 2016-2025). The APASTI 2016-2025 aims at intensifying R&D collaboration between the public and private sector, strengthening ST&I infrastructure and human resources, networking research institutes and centres across ASEAN, and promoting closer cooperation in R&D with ASEAN's Dialogue Partners.²²

The ASEAN Secretariat has also established international collaborations in R&D. Thus, in 2020, the United States launched the *US-ASEAN Health Futures Initiative* to strengthen public health in ASEAN through the development of R&D infrastructure, human capital, and health system capacity. As part of the *Initiative*, there are now more than 300 joint projects between ASEAN members and the US NIH. The *Initiative* includes US\$ 30 million over the last 10 years in grants to research institutions in ASEAN, and technical support for clinical trials for treatment of infectious diseases.²³ Likewise, the United States Center for Disease Control and Prevention (CDC) established the *US-ASEAN Infection Prevention and Control Task Force*.²⁴

Meetings among key stakeholders in vaccine R&D in ASEAN (health policymakers, biomedical researchers, and the pharmaceutical industry) sponsored by the *Southeast Asian Ministers of Education Organisation* (SEAMEO) *Tropical Medicine Network* identified

dengue, HPV, HIV, malaria, Japanese encephalitis, leptospirosis, and influenza as the key regional R&D priorities.²⁵ Likewise, expert group meetings convened by the WHO have identified key areas for ASEAN collaboration and integration in vaccine R&D; namely, vaccine security and self-reliance, human resource capacity building, pooled vaccine procurement, and communication and coordination.²⁶

Regional cooperation in vaccine R&D has also taken place outside the framework of supranational and intergovernmental organisations. Three of them deserve to be noted here. First, the *Association of Academies and Societies of Sciences in Asia* (AASSA), which comprises 32 ST&I societies from 30 Asian countries, including two from Thailand: the Thai Academy of Sciences, and the Science Society of Thailand.²⁷ In the context of the COVID-19 pandemic, AASSA organised webinars but, compared to similar organisations elsewhere, AASSA has played a relatively low-key role. Second, the *Southeast Asia Infectious Disease Clinical Research Network* (SEAICRN), a partnership between hospitals and research institutions in Thailand, Viet Nam, and Indonesia, which promotes clinical research collaborations on emerging infectious diseases of public relevance.²⁸ SEAICRN receives financial and technical support from the NIH in the USA, the Wellcome Trust in the UK, and the governments of Thailand, Viet Nam and Indonesia. Third, the *ASEAN Network for Drugs, Diagnostics, Vaccines and Traditional Medicines Innovation* (ASEAN-NDI), which has the support of the WHO, maps the overall research capacity of ASEAN countries in vaccines, drugs, traditional medicines, and diagnostic tools.²⁹ The ASEAN-NDI aims *inter alia* at strengthening cooperation between ASEAN countries in health R&D, sharing information on infectious diseases, transferring knowledge and/or technology, and facilitating collaboration in R&D initiatives.

CONCLUSION

As an upper-middle income country, Thailand has the financial and technological capabilities, in cooperation with other ASEAN countries, to ensure its national and regional vaccine security. Still, there are several actions at the national and regional levels that can enhance incentives for pharmaceutical firms to invest in vaccine R&D.³⁰ On the supply-side, Thailand and other ASEAN governments can incentivise vaccine R&D by mobilising financial and scientific resources for R&D on vaccines for diseases posing a domestic or regional public health threat. Thailand can also use other supply-side mechanisms, such as regulatory, policy, tax, and direct subsidies to reduce investment risks for pharmaceutical firms. On the demand-side, Thailand can strengthen policies and regulations to increase the uptake of vaccines through public information campaigns.

Partnerships between universities and the pharmaceutical industry are key sources of innovation. Thailand can promote new alliances and strengthen existing ones through a series of actions. Some of them require increasing financial resources for R&D; for example, such as the establishment of start-up incubators or the financing of joint projects between universities and public research institutes, and pharmaceutical firms. However, others involve regulatory and legislative reforms; for example, better defining the intellectual property rights of pharmaceutical companies and academic institutions for knowledge sharing and technology transfer, allowing academic researchers to carry out projects in pharmaceutical firms, or

facilitating cross-participation of academic researchers and industry leaders on corporate and university boards.

Finally, at the regional level, ASEAN as a group, rather than Thailand alone, can pool financial resources to establish advanced purchase commitments with pharmaceutical firms for the R&D and manufacturing of vaccines against diseases of regional concern.

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