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LETTER

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Global extension of Japanese medical products related to COVID-19: A survey of WHO Emergency Use Listing

Mami Wakabayashi[1,*], Yasunori Ichimura[2], Eiichi Shimizu[2], Tomoko Nishioka[2], Yuzuru Kono[2], Masahiko Doi[2], Yuriko Egami[2], Tomoka Kadowaki[3], Hiroyasu Iso[1,4], Noriko Fujita[2]

[1] Institute for Global Health Policy Research, Bureau of International Health Cooperation, National Center for Global Health and Medicine, Tokyo, Japan;

[2] Bureau of International Health Cooperation, National Center for Global Health and Medicine, Tokyo, Japan;

[3] Department of Epidemiology, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Okayama, Japan;

[4] Public Health, Department of Social Medicine, Osaka University Graduate School of Medicine, Osaka, Japan.

Abstract: The World Health Organization (WHO) has been utilizing Emergency Use Listing (EUL) to expand access to medical products during the COVID-19 pandemic. EUL is a risk-based procedure for assessing and listing unlicensed vaccines, medicine, and *in vitro* diagnostics. To determine whether Japanese medical products acquired EUL relating to COVID-19, we conducted desk research as a part of a new project. Results showed that thirteen of twenty-eight *in vitro* diagnostic products were from China and three of ten vaccines on EUL were from India. However, only one vaccine manufactured in Japan was on EUL. A common weakness of Japanese companies in the global public procurement market was a lack of knowledge on qualification systems for medical products. We hypothesized holistic approaches from private companies and systematic supports from public sectors are required for a response to an emergency. These activities could lead to contribute to global health issues through sustainable businesses.

Keywords: global public procurement, vaccines, medicine, *in vitro* diagnostics, public-private partnership, international cooperation

The World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19) as a Public Health Emergency of International Concern (PHEIC) in January 2020 (*1*). In response to the pandemic, the development of medicines, vaccines, and *in vitro* diagnostics for COVID-19 began worldwide. The Emergency Use Listing (EUL) is a WHO procedure for assessing unlicensed medicines, vaccines, and *in vitro* diagnostics during a PHEIC to expedite the availability of these products to people who need them (*2*). The EUL was established and reformed by the Emergency Use Assessment and Listing mechanism which was developed to respond to the 2014-2016 Ebola virus disease outbreak (*3*). The EUL indicates certain standards for interim use of unlicensed products under emergencies. Therefore, pharmaceutical companies were competing for the development of COVID-19 products and submitting their product documentation for EUL to supply their products worldwide. However, before submitting documentation, the establishment of an assessment platform is necessary among the WHO, external experts, and the national regulatory authority (NRA) where the products produce. The EUL procedure is based on a public-private partnership.

The number of new COVID-19 cases in Japan was very low on the week of December 22, 2021, with about 0.9 per 100,000 and no cases in some regions (*4*). However, Japan also had the first report of a new SARS-CoV-2 variant belonging to the Pango lineage B.1.1.529 (Omicron variant) on December 6, which has spread rapidly in January (*5*). The number of new COVID-19 cases in Japan increased to 41 per 100,000 on the week of January 13, 2022 (*6*). The Omicron variant has been spreading rapidly around the world and 20 million new cases globally were confirmed on the week of January 10 (*7*). Considering the ongoing pandemic, the EUL should be continuously used to expand access to COVID-19 medical products.

The Bureau of International Health Cooperation, National Center for Global Health and Medicine (NCGM) conducted the preliminary result of a desk research to examine whether Japanese medical products acquired EUL relating to COVID-19.

By January 17, 2022, the Pharmaceutical and Medical Devices Agency (PMDA) responsible for approval of medicine or medical devices relating to COVID-19 in Japan approved 71 *in vitro* diagnostic products, 3 vaccines, and 5 medicines including special

approval which distributed by companies in Japan (*8*). Meanwhile, 28 *in vitro* diagnostic products, 10 vaccines, and no medicines were listed on the EUL (Figure 1).

Table 1 shows the countries of origin of developers who applied to EUL and were accepted on the list. In Table 1, we counted vaccines by the number of national authorities instead of the number of countries that developed the product because if the same vaccine was manufactured in other countries, a different application to EUL with each national authority's platform was still needed. *In vitro* diagnostic products by Chinese companies were the most frequently accepted among 74 applications to EUL, followed by American companies. Vaccines by Indian companies were the most frequently accepted among 29 applications on EUL, followed by China, the U.S., Korea, and the Netherlands. Half as many vaccine applications compared to *in vitro* diagnostics for EUL were listed by January 17, 2022. This may reflect the complexity of products and the assessment process for vaccines (*9*), while there were 140 vaccine candidates in clinical trials in the world (*10*).

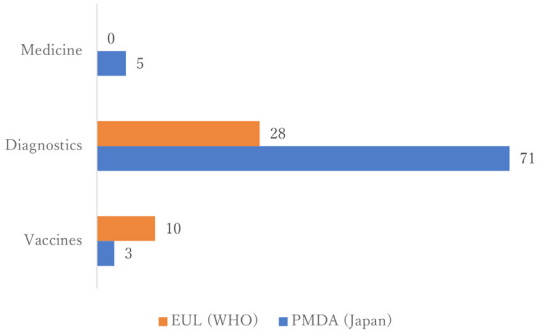

Figure 1. The number of medical products related to COVID-19 by qualification as of January 17, 2022 (date of data accession). Data are updated irregularly. PMDA: Pharmaceutical and Medical Devices Agency of Japan; EUL: Emergency Use Listing by World Health Organization.

Forty-eight products from China underwent application for the EUL, which is four times that from the U.S., although the acceptance proportion in China was much lower than that for U.S. products (Table 1). This may be a result of the "Made in China 2025 (MIC25)" policy (*11*). The MIC25 policy was launched in 2015 by Xi Jinping, the party and state leader of China. The strategy defined ten core industries, including biomedicine and high-performance medical equipment aimed at boosting local capabilities. Furthermore, more than 1,800 government industrial investment funds were invested in MIC25 with 3 trillion CNY in March 2018 (*11*). MIC25 encourages the development of key biopharma clusters to accelerate innovative research and clinical trials (*12*).

Table 1. The number of products categorized by the countries of origin of product developers on Emergency Use Listing as of January 17, 2022 (date of data accession)

Countries	Diagnostics (Total: 74)		Vaccines (Total: 29)			
	Accepted	Not accepted	Accepted (The name of vaccine)	In process	Total	Acceptance proportion (%)
China	13	28	2 (Coronavac, ShinophamBIBP)	5	48	31
United States	7	2	2 (Comirnary, Spikevax)	0	11	82
India	1	3	3 (Covishield, Covaxin, Covovax)	1	8	50
Korea	3	3	2 (Vaxzevria, Spikevax)	0	8	63
Germany	2	3	1 (Comirnaty)	0	6	50
United Kingdom	1	1	0	0	2	50
Japan	0	1	1 (Vaxzevria)	0	2	50
Netherlands	0	0	2 (Ad26.COV2-S, Nuvacovid)	0	2	100
Turkey	1	1	0	0	2	50
Vietnam	0	2	0	0	2	0
Italy	0	2	0	0	2	0
Russia	0	0	0	2	2	0
Spain	0	0	1 (Spikevax)	0	1	100
Australia	0	0	1 (Vaxzevria)	0	1	100
Sweden	0	0	1 (Vaxzevria)	0	1	100
France	0	0	0	1	1	0
Cuba	0	0	0	1	1	0
Canada	0	0	1 (Vaxzevria)	0	1	100
Mexico	0	0	1 (Vaxzevria)	0	1	100
Argentina	0	0	1 (Vaxzevria)	0	1	100
Total	28	46	19	10	103	

Footnote: Comirnaty was developed by BioNTech (Germany) and Pfizer (United States). Vaxzevria was developed by AstraZeneca and Oxford University in the United Kingdom. Spikevax was developed by Moderna Biotech (United States). We assigned each vaccine to its respective national authority listed on Emergency Use Listing. Vaccines approved by the European Medicines Agency (EMA) were assigned to the country or countries which applied to the EMA. There were many *in vitro* diagnostic products under review, which numbers were not counted in Table 1. We calculated the acceptance proportion based on our definition for this survey based on the latest available data from January 17, 2022. Data are updated irregularly.

Japanese companies rarely competed to apply for EUL, although there are 71 PMDA-approved *in vitro* diagnostic products in Japan. Only one vaccine produced by Japanese companies was on the EUL list, which was developed by AstraZeneca and Oxford University (*13*). Recent surveys showed that one of the common weaknesses of Japanese companies in the global public procurement market was a lack of knowledge about the qualification procedure for medical products (*14*) and a lack of understanding of global public procurement systems (*15*). Language barriers should also be considered. To fill the gap, the NCGM has implemented a series of seminars to introduce the qualification procedure, focusing on "prequalification" (PQ) as defined by the WHO. PQ is a systematic process to determine the capacity of a manufacturer to produce medical products of consistent quality in accordance with WHO specifications (*16*), which is utilized for general procurement. Compared with PQ, EUL focuses on only three categories of products (vaccines, medicines, *in vitro* diagnostics) for emergency procurement. The series of seminars related PQ is a part of activities supported by the projects for the global extension of medical technologies which have implemented since 2015 under the "Japan Revitalization Strategy" by the Government of Japan (*17*). These projects aim to disseminate Japanese medical technologies, high-quality medicines, medical devices, and health services in a way that suits local needs and to improve health and medical care in low- and middle-income countries. The project detail was available on the other paper (*17*).

Under the project newly granted from 2021 to 2023, we have analyzed the process for both global public procurement and emergency procurement related to COVID-19 and hypothesized that seven steps based on "the access and delivery partnership" approach are essential for both means of procurement (*18*). The seven steps are as follows: *i*) analysis of needs, *ii*) research and development, *iii*) regulatory approval, *iv*) selection and prioritization, *v*) procurement or bidding, *vi*) distribution and storage, and *vii*) service delivery. The integrated approach across the seven steps by private companies is necessary to drive successful global public procurement. We are continuing analysis of case studies to find out root causes and possible solutions or public-private interventions for joining the global public procurement and for quickly responding to global emergency procurement.

Only one vaccine produced by Japanese companies had EUL, which was developed by AstraZeneca and Oxford University. Moreover, Japanese companies seem to not be successful when applying for general global public procurement related to COVID-19 (*19*). Several successful Japanese companies for global public procurement under COVID-19 were continuously preparing before the pandemic. To encounter current and future public health emergencies, basic preparation for global public procurement will help during emergency procurement procedures including applying to EUL. Further systematic supports from the public sectors to private companies are needed to enter the global public procurement market. The Government of Japan established the "Global Health Strategy Promotion Council" under the Prime Minister of Japan and the Cabinet to strengthen global health strategy in 2021 (*20*). Japan will determine how they can contribute to global health issues through enhancing sustainable business and public-private partnerships.

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Conflict of Interest: The authors have no conflicts of interest to disclose.

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**Address correspondence to*:
Mami Wakabayashi, Institute for Global Health Policy Research, Bureau of International Health Cooperation, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan.
E-mail: mwakabayashi@it.ncgm.go.jp