Global Health & Medicine. 2022; 4(2):144-145.
LETTER
DOI: 10.35772/ghm.2022.01023

Establishment of an emergency regulatory approval system in Japan in response to the COVID-19 pandemic and challenges in developing domestically produced vaccines

Mugen Ujiie*

Vaccination Support Center, National Center for Global Health and Medicine, Tokyo, Japan.

Abstract: Although ten vaccines against novel coronavirus infection (COVID-19) have been placed on the World Health Organization (WHO)'s emergency use list, no vaccine has been developed by Japanese pharmaceutical companies. As of March 2022, 10 billion doses of vaccines have been administered worldwide 2 years after the infection was declared a pandemic by the WHO. Japan lacks a system for approval of pharmaceuticals at the stage of presumed efficacy in emergencies, such as the COVID-19 pandemic. The absence of such an emergency approval mechanism is believed to have been a stumbling block to the rapid availability of urgently needed drugs. Further promotion of vaccine development in Japan will require comprehensive improvement of investment in the vaccine field, which is critically lacking from a long-term perspective.

***Keywords*:** vaccine development, Japan, COVID-19 pandemic, emergency approval system

Two years have passed since March 11, 2020, when the Director-General of the World Health Organization (WHO) declared the novel coronavirus infection (COVID-19) a pandemic (*1*). Many vaccines and therapeutics are now available; however, regional inequality in access to medicines is a global problem. Ten vaccines have already been placed on the WHO's emergency use list. As of January 2022, 1 billion doses of vaccines had been supplied to low- and middle-income countries through the COVID-19 Vaccines Global Access (COVAX). In addition, more than 10 billion doses of vaccines have been administered worldwide as of March 2022 (*2*). Nevertheless, no COVID-19 vaccine has been developed by Japanese pharmaceutical companies, and the only vaccine in Phase III clinical trials is a recombinant protein vaccine (S-268019) developed by Shionogi Inc (*3*).

In Japan, the manufacture and sale of pharmaceuticals and medical devices are approved under the Pharmaceuticals and Medical Devices (PMD) Act. In emergencies, such as the COVID-19 pandemic, there is no system for approval of pharmaceuticals at the stage of presumed efficacy in Japan, as is the case with the Emergency Use Authorization (EUA) system in the United States. Currently, newly developed drugs have been approved under the framework of "special approval". This system is applicable only when the following three conditions are met: *i*) The drug is urgently needed to prevent the spread of a disease that may seriously affect the lives and health of the Japanese people; *ii*) There are no other alternative measures available; and *iii*) The quality of the drug is systematically guaranteed on a par with that in Japan.

The product must already be approved for manufacture and sale in a foreign country. In the current outbreak, foreign countries in this condition were defined as the United States, the United Kingdom, Canada, Germany, and France. The absence of such an emergency approval mechanism is believed to have been a stumbling block to the rapid availability of urgently needed drugs (*4*). Pfizer's COVID-19 vaccine was approved for emergency use in the United States on December 11, 2020, but was granted special exception approval in Japan on February 14, 2021. In light of this, a draft amendment to the PMD Act to allow for emergency regulatory approvals was submitted to the Diet on March 1, 2022, for deliberation (*5*). The outline of the revised law is as follows: *i*) The drug must be used urgently to prevent the spread of a disease or other health hazard that may seriously affect the lives and health of the public; *ii*) No other alternative means exist. However, a time limit is given for approval, and confirmation of efficacy is required within the time limit, or the approval will be revoked. Reports of adverse reactions are collected under the existing reporting system and compensated under the Adverse Reaction Relief System.

If this emergency approval legislation is enacted, it will allow for more rapid use of drugs with

presumable efficacy under the system. However vaccine development challenges remains a response to the COVID-19 pandemic. First, since several vaccines and therapeutics have already been approved under the notable exception, alternative methods being established would not meet the requirements for emergency approval. Second, the evaluation of efficacy based on presumption would need to be executed with considerable caution. If efficacy is not confirmed after emergency approval, the effort in making the drug widely available would have been wasted, and the issue of adverse reactions may be brought into greater focus. There is also a risk that this could lead to a loss of confidence in the regulatory system and science, adversely affecting the credibility of drugs approved under other standard systems.

In the strategy for strengthening vaccine development and production systems approved by the Cabinet last June (*6*), it was noted that there was a critical lack of investment in the vaccine sector, as a long-term, ongoing national strategy to be implemented by the government as a whole. In addition, the goal is to ensure that the necessary financial resources are secured on a continuous and stable basis in regular times, including flexible and rapid funding in times of emergency, arrangements on how funds are allocated, research and development expenses, equipment maintenance expenses, and the purchase of vaccines in development. In these ways, measures are being taken to address the delay in vaccine development in Japan experienced during the COVID-19 pandemic against the next pandemic that is sure to occur in the future. Continuous monitoring is required to ensure that the stakeholders in vaccine development can steadily implement improvements based on the plan.

Funding: None.

Conflict of Interest: The author has no conflicts of interest to disclose.

References

1. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020, 2020. *https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020* (accessed March 14, 2022)
2. World Health Organization. COVID-19 vaccines WHO EUL issued, 2022. *https://extranet.who.int/pqweb/vaccines/vaccinescovid-19-vaccine-eul-issued* (accessed March 14, 2022)
3. ClinicalTrials.gov [Internet]. National Library of Medicine (US). Identifier NCT05212948, A Study of S-268019 for the Prevention of COVID-19. *https://clinicaltrials.gov/ct2/show/NCT05212948* (accessed March 14, 2022)
4. Ministry of Health, Labour and Welfare. Enforcement of the Cabinet Order for Partial Revision of the PMD Act Implementation Order, Notice of May 2, 2020. *https://www.mhlw.go.jp/content/000627465.pdf* (accessed March 14, 2022) (in Japanese)
5. Ministry of Health, Labour and Welfare. The 208th Congress of Japan Presenting Legal Cases. *https://www.mhlw.go.jp/stf/topics/bukyoku/soumu/houritu/208.html* (accessed March 14, 2022) (in Japanese)
6. Prime Minister of Japan and the Cabinet. Strategy to strengthen vaccine development and production system, 2021. *https://www.kantei.go.jp/jp/singi/kenkouiryou/tyousakai/dai28/siryou1-2.pdf* (accessed March 14, 2022) (in Japanese)

Received March 17, 2022; Revised April 4, 2022; Accepted April 6, 2022.

Released online in J-STAGE as advance publication April 9, 2022.

**Address correspondence to*:
Mugen Ujiie, Vaccination Support Center, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku, Tokyo 162-8655, Japan.
E-mail: mgujiie@hosp.ncgm.go.jp