

CoRE Regulatory Perspective

Making Sense of Emergency Use Authorisations (EUAs) for Covid-19 Vaccines and Considerations for the Road Ahead

9 December 2020

The Medicines & Healthcare products Regulatory Agency (MHRA) in the United Kingdom (UK) granted emergency use authorisation (EUA) to the Covid-19 vaccine BNT162b2 supplied by Pfizer and BioNTech under Regulation 174 of the Human Medicine Regulations 2012 on 2 December 2020¹. This followed the previous authorisations for Covid-19 vaccines by China and Russia for their own vaccines. The recent announcements have created great hope for a path out of this global pandemic. This brief article seeks to demystify the concept of EUAs and highlight some important considerations as we can expect more submissions for Covid-19 vaccine authorisations in the near future. Our key take-away is that although emergency use authorisations are temporary and subject to ongoing data reviews, regulatory agencies follow rigorous evidence-based approaches to ensure the safety of vaccines authorised using this pathway.

What is an emergency use authorisation?

An Emergency Use Authorisation (EUA) is a regulatory mechanism to facilitate the availability and use of medical countermeasures, including unapproved or investigational health products, during public health emergencies, such as the current Covid-19 pandemic². National Regulatory Authorities (NRAs) can issue an EUA when certain legal criteria have been met such as a national health emergency and/or no adequate, approved, and available alternatives. It is not just NRAs that can use emergency use mechanisms. After the experience during the West African Ebola outbreak from 2013-2016, the World Health Organisation (WHO) developed the Emergency Use Assessment and Listing (EUAL) procedure for health products which was updated in January 2020 with the Emergency Use Listing (EUL) procedure³.

The specific conditions of emergency use mechanisms may differ among jurisdictions and in some jurisdictions similar regulatory mechanisms may have different names. A common element of most emergency use procedures is an assessment of whether submitted (and frequently limited) data demonstrate a reasonable likelihood that a product's quality, safety, and efficacy are acceptable, and that the benefits outweigh potential risks and uncertainties in the context of a public health emergency of national or international concern³.

The authorisation recently announced in the United Kingdom under Regulation 174 is temporary and only relates to a limited number of specific batches of the Covid-19 vaccine BNT162b2 supplied by Pfizer and BioNTech, in response to the increased spread of Covid-19 and deaths in the UK. This emergency approval is not a market authorisation and there is no general authorisation to place this vaccine on the market in the UK. However, the conditions of the EUA stipulate that the sponsor "must operate a comprehensive pharmacovigilance (safety monitoring) system for this product in accordance with UK legislation for licensed products, as if they were market authorisation holders."⁴ This clause ensures that processes are in place to monitor

changes in the benefit-risk profile of the vaccine, and facilitate timely revisions to its use if required.

Why was the MHRA able to give an EUA faster than US FDA or EMA?

Although this question has been a focus of discussions since the UK EUA announcement, it is important to note that countries are not in a race against each other.

According to the MHRA, they undertook a rolling review of the data since the first data was made available in October 2020 to allow for the assessment of the vaccine in the shortest possible time⁵. The UK had also prepared its safety surveillance systems, expert working groups and public health laboratories batch testing procedures months before⁶. The UK remains under the authority of the EU's European Medicines Agency (EMA) until the end of the Brexit transition on 31 December 2020 but have used a provision in UK and EU law that allows member states to “temporarily authorise the distribution of an unauthorised medicinal product in response to the suspected or confirmed spread of pathogenic agents, toxins, chemical agents or nuclear radiation any of which could cause harm”⁷. Any EU member state could legally use that provision to make an independent decision from the EMA approach for a Covid-19 vaccine. For now, most member states have aligned with the overall EU strategy, which is to subject any investigational COVID-19 vaccines for the European market to EMA's conditional or full marketing authorisation rather than invoke emergency authorisations in each EU member state⁸.

EMA is accepting rolling submissions for Covid-19 vaccines under the conditional marketing authorisation (CMA) procedures and is expected to announce a decision on the Pfizer/BioNtech vaccine after its scientific committee for human medicines meets on 29 December 2020. EMA can grant CMA for such health products where “the benefit of immediate availability outweighs the risk of less comprehensive data than normally required, based on the scope and criteria defined in legislation and guidelines.”⁹ The data requirements for products intended for use in emergency situations are less comprehensive for both clinical and non-clinical data⁹. The CMA is valid for a year and can be renewed annually. The EMA has stated that the CMA it plans to grant would require more data than the emergency use authorisation issued by the MHRA⁸.

The Pfizer/BioNtech vaccine has also been submitted for EUA to the United States Food and Drugs Administration (US FDA). The US FDA required two months of safety data for at least half the patients in a study before a company could even submit for authorisation¹⁰. The US FDA has not assessed the data on a rolling basis as their counterparts in the UK and Europe. For routine new drug approvals, the US FDA typically will require all the raw data from a sponsor and perform their own patient-

level analysis of the data, while MHRA and EMA would not systematically perform such analysis. This type of detailed analysis, routine for new drug approvals at the US FDA, is not legally necessary for US EUAs during a pandemic¹⁰. The agency opted for a more thorough review given the larger population that would be potentially receiving this vaccine and this may also be useful to address vaccine hesitancy concerns. The US FDA report of its detailed analysis of the Pfizer and BioNTech vaccine data, released on 8 December 2020, states that the vaccine has met the success criteria for safety and efficacy ahead of the planned FDA advisory committee meeting on 10 December¹¹. A similar committee will convene on 17 December to consider the EUA of the Moderna vaccine.

Although there have been slight differences in how agencies have approached the EUA procedures, the monitoring for long-term safety and efficacy among countries is likely to follow similar principles and all three agencies in the EU, the UK and the US have strong systems for pharmacovigilance and adverse event monitoring.

Do NRAs in the Asia-Pacific region have provisions to allow similar emergency authorisations?

Many countries in the Asia-Pacific region have their own emergency use authorisation procedures to allow access to investigational health products during health emergencies. In Singapore, the Health Sciences Authority has a Pandemic Special Access Route (PSAR) which may be used to grant interim authorisation to therapeutic products during the pandemic where there is reasonable evidence suggesting that the potential benefits outweigh the risks for their use in treating or preventing a disease in an emergency that may pose serious threats to the public¹². Australia's Therapeutic Goods Administration is using the provisional approval pathway to allow temporary registration of Covid-19 vaccines¹³. Philippines President Duterte has recently signed an executive order enabling the Philippines Food and Drug Administration to give emergency use authorisations for Covid-19 drugs and vaccines on 1 December 2020¹⁴.

Regulatory agencies accepting emergency use applications will require on-going quality, safety and efficacy data generated to support the eventual transition of the interim authorisation to market authorisation. The agencies also reserve the right to withdraw the temporary authorisation should any issues with quality, safety and efficacy be identified in future data. As for all health products, the EUAs and market authorisations should be evidence-based, using available science and data.

Considerations for EUAs for COVID-19 vaccines in the future

EUAs are a powerful tool in the public health response arsenal for countries during this pandemic. However, it is important to understand that unlike full market authorisation, they do not make Covid-19 vaccines generally available to the whole population in the same way as influenza vaccines. Rather, they allow governments to deploy available new vaccines as quickly as possible to specific groups of the most vulnerable people such as frontline healthcare workers, older people and other high-risk groups while collecting important data on the novel vaccines to make decisions about broader immunisation programmes.

Experts have warned of the potentially negative influence of national politics on global vaccine efforts, as countries race to be “first” to approve vaccines and therapeutics, that could damage trust in the integrity of the EUA procedures and contribute to vaccine hesitancy³. Support for using EUAs for Covid-19 vaccines is not unanimous. There are some concerns that authorising vaccines through an EUA rather than full market authorisation could make it difficult to complete clinical trials of the involved vaccines and could hamper the ability to effectively compare vaccine candidates to determine which ones have more favourable benefit-risk profiles in different populations¹⁵. Ethical questions have also been raised about whether trial participants who received the placebo should be “unblinded” and offered the provisionally authorised vaccines¹⁶. Community engagement to increase understanding about the vaccine development and approval process is key to promoting trust in the vaccines.

There is wide variation in the capacity to carry out post-licensure vaccine safety surveillance between countries and a collaborative global approach to support monitoring in lower and middle income countries should be a priority¹⁷. Regulatory agencies should continue to cooperate, share information and leverage reliance best practices to ensure timely access to Covid-19 vaccines and adhere to similar frameworks for monitoring safety and efficacy of these vaccines to facilitate full marketing authorisation to the wider population and long-term post-market pharmacovigilance monitoring.

Author

Dr Nokuthula Kitikiti, Public Health Physician

with inputs from

Assistant Prof James Leong, Head of Regulatory Science Programme

Prof John Lim, Executive Director

Centre of Regulatory Excellence (CoRE)

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Contact us

Tel: +65 6601 5147

Email: CoRE@duke-nus.edu.sg



Duke-NUS Medical School
8 College Road
Singapore 169857

www.duke-nus.edu.sg/core



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