Received: 14 May 2021 | Revised: 8 June 2021 | Accepted: 19 June 2021

DOI: 10.1111/all.14995

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI WILEY

EDITORIAL

COVID-19 vaccines—The way forward

In a health crisis of the calibre of the COVID-19 pandemic, the development of effective and safe vaccines is considered the most powerful measure to save lives and minimize the tremendous negative impact on health, social systems and global economics.

Vaccines must be evaluated and approved by the appropriate regulatory and/or health authorities. To date, the worldwide regulatory landscape for vaccines is very broad. Bringing COVID-19 vaccines to the market, the authorities followed at least 51 different pathways, offering various types of accelerated vaccine approval.[1] China, Russia and the United Arab Emirates initiated the vaccine administration before the conclusion of clinical trials. This patchwork of approval processes has revived a long-standing question, how to better facilitate harmonization in vaccine regulation and whether a harmonized approval process would make the vaccine development procedures more effective, quicker, broadly accessible and administered by the whole world and even less expensive. In this issue, experts from the Paul-Ehrlich Institute, the regulatory institution for vaccine development in Germany, describe the regulatory procedures, concepts and requirements that are applied to guide and promote the accelerated development and licensure of safe and efficacious COVID-19 vaccines in Europe.[2]

Vaccine regulation worldwide began in the USA, when on 1st July 1902, the U.S. Congress passed 'An act to regulate the sale of viruses, serums, toxins, and analogous products', later referred to as the 'Biologics Control Act' that established the government's right to control the manufacturing of vaccines. This is now regarded as the first modern federal legislation to control the quality of drugs and emerged in part as a response to 1901 contamination events in St. Louis and Camden involving smallpox vaccine and diphtheria antitoxin. It created the Hygienic Laboratory of the U.S. Public Health Service that eventually became the National Institutes of Health and set up the FDA in 1906, the world's oldest national medicine regulator.

In the European Union (EU), the European Medicines Agency (EMA) supervises the regulation of vaccines and other drugs. Europe's regulatory system comprises the network of 50 national regulatory bodies from 30 European countries. All countries have their own national regulatory authorities, but if Europe-wide approval is required, the EMA provides manufacturers with a unique place for the scientific evaluation of d\rug applications.

African countries are also inching towards an approach that allows for the pooling of regulatory expertise since 2006 in the African Vaccine Regulatory Forum.[3] Similarly, in Australia, any COVID-19 vaccine candidate must meet the well-established and rigorous assessment and approval processes of the Therapeutic Goods Administration (TGA) within the Department of Health.[4]

Many countries worldwide adopted the standards of the World Health Organization and ICH for biological products. These include a set of legal, administrative and technical/measures to ensure safety, efficacy and quality of approved vaccines. They can vary from country to country, both in the scope and implementation, but generally include at least the following functions (WHO 2021)[5]:

- licensing the manufacture, import, export, distribution, promotion and advertising of vaccines;
- assessing the safety, efficacy and quality of vaccines, and issuing marketing authorization;
- Inspecting, and conducting surveillance of, manufacturers, importers, wholesalers and dispensers of vaccines;
- controlling and monitoring the quality of vaccines existing on the market;
- controlling the promotion and advertising of vaccines;
- monitoring adverse reactions related to the vaccines in use;
- providing independent information on vaccines to the professionals and the public.

Progress in vaccine regulation globally includes a shift towards strictly defined procedures for vaccine consistency, reliance on Good Manufacturing Practices (GMPs) along with final product testing and continued vaccine pharmacovigilance.

So far, the EU granted a conditional marketing authorization (CMA) to four COVID-19 vaccines and four other vaccine candidates are under rolling review at the EMA.[2] A CMA can be issued for vaccines in emergency situations as a valuable option to expedite vaccine licensure with postponement of some data requirements but based on the reliable demonstration of a positive benefit-risk balance.[2] Moreover, procedural timelines for data evaluation were drastically reduced and the regulatory assessment at the EMA and FDA was further expedited by applying a 'rolling review' approach allowing for a very flexible and time-optimized processing and assessment of individual data packages immediately upon their availability. However, faster approvals must never lead to a reduction in safety.[6] Existing regulatory requirements and procedures were wisely and carefully adapted without compromising the thoroughness of the regulatory and scientific assessment. The concerted activities of scientists, manufacturers and regulators led to the development and licensure of novel COVID-19 vaccines in an unprecedentedly fast

and flexible manner within <1 year. Extensive data collection from the field is ongoing with the highest priority to detect and mitigate any possible adverse effects.[7,8]

Globally, a number of other vaccine candidates are presently under development at different stages of clinical exploration. Global harmonization of vaccine regulation would be very beneficial. It has to be strongly considered that in such a fast-moving pandemic, no one is safe unless everyone is safe, so work for global equitable access to COVID-19 vaccines through COVAX, an initiative that aims to ensure equal and equitable access to COVID-19 vaccines worldwide, should be strongly supported. This pandemic can only be overcome by extensive vaccination of the whole world. In addition, this extensive vaccination should be done as fast as possible to avoid mutations and formations of new vaccine-resistant variants of SARS-CoV-2.[9] Pharmaceutical industry could use agreed definitions for different types of approval and harmonized guidelines including animal models for testing COVID-19 vaccines, the optimal clinical-trial end points and better facilitate their applications. Regulators share data, assessments and compare findings and analyses in order to achieve better decision taking. For example, pharmacovigilance benefit from collaborative monitoring as faint signals of adverse effects might be too weak to detect in a single country or region. In this way, public confidence could rise and counteract vaccine hesitancy. WHO initiatives, and the International Coalition of Medicines Regulatory Authorities (ICMRA), including regulators from China, Europe and the United States, may open the best way forward.

KEYWORDS

COVID, SARS-CoV, virus

CONFLICT OF INTEREST

Dr. Klimek reports grants and/or personal fees from Allergopharma, MEDA/Mylan, HAL Allergie, ALK Abelló, LETI Pharma, Stallergenes, Quintiles, Sanofi, ASIT biotech, Lofarma, Allergy Therapeut., AstraZeneca, GSK, Inmunotk, Cassella med, outside the submitted work; and Membership: AeDA, DGHNO, Deutsche Akademie für Allergologie und klinische Immunologie, HNO-BV, GPA, EAACI. Dr. Cooke reports to be a Member of the European Medicines Agency, Amsterdam, Netherlands. Dr. Jutel reports personal fees from ALK-Abello, Allergopharma, Stallergenes, Anergis, Allergy Therapeutics, Leti, HAL, during the conduct of the study; personal fees from GSK, Novartis, Teva, Takeda, Chiesi, outside the submitted work. Dr. Akdis reports grants from Allergopharma, Idorsia, Swiss National Science Foundation, Christine Kühne-Center for Allergy Research and Education, European Commission's Horison's 2020 Framework Programme, Cure, Novartis Research Institutes, Basel, Astra Zeneca, Switzerland, Scibase, Stockholm, advisory role for Sanofi/Regeneron, Glaxo Smith-Kline, Novartis. Dr. Agache and Dr. O'Hehir have nothing to disclose.

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