COVID-19 vaccines: Safety Surveillance Manual

Module: Introduction

Table of contents

Background

On 30 January 2020, the World Health Organization (WHO) declared that the outbreak due to a novel coronavirus, SARS-CoV-2, also known as COVID-19, is a public health emergency of international concern (PHEIC). By 12 March 2020, due to its rapid global spread, the outbreak was declared a pandemic. The global pandemic has already caused the loss of more than one million of lives and disrupted the lives of billions more.

One key and critical strategy in containing this pandemic is the rapid development of safe and effective vaccines. Unprecedented efforts are being made to develop large number of vaccines simultaneously in a short time. Global equitable access to a vaccine, particularly protecting health care workers and those most-at-risk is one of the key strategies to mitigate the public health and economic impact of the pandemic.

The Access to COVID-19 Tools (ACT) Accelerator was launched at the end of April 2020 as a global collaboration to accelerate development, production, and equitable access to COVID-19 tests, treatments, and vaccines. It brings together governments, scientists, businesses, civil society, and philanthropists and global health organizations (the Bill & Melinda Gates Foundation, CEPI, FIND, Gavi, The Global Fund, Unitaid, Wellcome, WHO, and the World Bank). The COVAX Facility offers participant countries secure access to safe and effective COVID-19 vaccines through its actively managed portfolio of vaccine candidates across a broad range of technologies. Its goal is to ensure equitable access to vaccines to all economies and ensure that income is not a barrier to access. The initial aim is to have 2 billion doses of vaccine available by the end of 2021.

The 42nd Global Advisory Committee on Vaccine Safety (GACVS) virtual meeting on 27–28 May 2020 addressed pharmacovigilance preparedness for the launch of the future COVID-19 vaccines. One of their recommendations was that infrastructure and capacity for surveillance of the safety of COVID-19 vaccines should be in place in all countries and existing infrastructure be reactivated and engaged before a vaccine is introduced. This will require local, national, regional and global collaboration. Countries should include preparedness plans for COVID-19 vaccine safety in their overall plans for vaccine introduction, building on WHO guidance. This COVID-19 vaccine safety guidance manual has been developed upon recommendation and guidance of GACVS members, as well as by experts incorporating current and available information critical to all stakeholders when COVID-19 vaccines will be introduced.

Lessons learnt from novel vaccine introduction during pandemic and epidemic emergencies

Key lessons learnt from past situations where new vaccines have been introduced in response to pandemic and epidemic emergencies been included in this guidance. For example, the 2009 H1N1 influenza pandemic demonstrated that few countries had a pandemic preparedness plan that

comprehensively addressed vaccine deployment and monitoring of adverse events. [1,2,] When adverse events were reported, the existing systems were unable to confirm or deny the association of the events with H1N1 vaccination leading to lack of confidence in H1N1 vaccination which was challenging for communication.[3,4]

The 2014-2016 Ebola epidemic that affected three countries in West Africa led to an accelerated development of vaccines and therapeutics. The African Vaccine Regulatory Forum, a regional network of regulators and ethics committees, working closely with regulators from other parts of the world helped reviews of clinical trial protocols and results, joint monitoring of trials and joint authorization and deployment of vaccines. [5,6] Such models can be used to guide pharmacovigilance reliance for the deployment of COVID-19vaccines, particularly in low-to-middle income countries with limited resources.

The introduction of the first licensed dengue vaccine, while not in the context of an international public health emergency, illustrated a number of lessons for the pharmacovigilance of novel vaccines, particularly the observed immune-enhanced disease which could be potentially associated with some of the COVID19 vaccine candidates being developed.[7,8]

A common theme in these examples is the public concerns about the safety of the novel vaccines and rumours that can arise during the current and future pandemics and the need for programme managers to be ready to address them through appropriate vaccine safety surveillance and communication strategies.

Objectives of this manual

The objectives of this manual are:

- to provide an overview of COVID-19 vaccines likely to be available and their characteristics;
- to identify the safety implications for the potential priority populations and immunization strategies;

---

[1] WHO. Main operational lessons learnt from the WHO pandemic influenza A(H1N1) vaccine deployment initiative. Available from: https://apps.who.int/iris/handle/10665/44711. Accessed 26 October 2020.

[2] European Medicines Agency. Pandemic report and lessons learned: outcome of the European Medicines Agency's activities during the 2009 (H1N1) flu pandemic. Available from: https://www.ema.europa.eu/documents/report/pandemic-report-lessons-learned-outcome-european-medicines-agencys-activities-during-2009-h1n1-flu_en.pdf. Accessed 26 October 2020.

[3] Sturkenboom MC. The narcolepsy-pandemic influenza story: can the truth ever be unravelled? Vaccine. 2015;33(Suppl 2):B6-B13

[4] Ropero-Álvarez AM, Whittembury A, Bravo-Alcántara P, Kurtis HJ, Danovaro-Holliday MC, Velandia-González M. Events supposedly attributable to vaccination or immunization during pandemic influenza A (H1N1) vaccination campaigns in Latin America and the Caribbean. Vaccine. 2015 Jan 1;33(1):187-92. doi: 10.1016/j.vaccine.2014.10.070.

[5] Akanmori B et al. The African Vaccine Regulatory Forum (AVAREF): A platform for collaboration in a public health emergency. WHO Drug Information 2015;29:127-132.

[6] Kieny MP, Rägo L. Regulatory policy for research and development of vaccines for public health emergencies, Expert Review of Vaccines 2016;15:1075-1077. DOI: 10.1080/14760584.2016.1188695.

[7] Flasche S, Wilder-Smith A, Hombach J, Smith PG. Estimating the proportion of vaccine-induced hospitalized dengue cases among Dengvaxia vaccinees in the Philippines. Wellcome Open Res. 2019 Oct 31;4:165. doi: 10.12688/wellcomeopenres.15507.1.

[8] Dayrit MM, Mendoza RU, Valenzuela SA. The importance of effective risk communication and transparency: lessons from the dengue vaccine controversy in the Philippines. J Public Health Policy. 2020 Sep;41(3):252-267. doi: 10.1057/s41271-020-00232-3.

- to identify all stakeholders, including vaccine marketing authorisation holders, and provide guidance on how they can collaborate to ensure the transparent collection, analyses and sharing of COVID-19 vaccine safety data
- to define the elements of COVID-19 vaccine pharmacovigilance preparedness and to identify current capacities and gaps in countries;
- to provide guidance for enhancing and harmonizing vaccine safety surveillance systems, to guide processes for collecting, analysing and sharing safety data and information, including data management systems;
- to support evidence-based programmatic decisions related to COVID-19 vaccines;
- to provide guidance to support vaccine safety communication during COVID-19 pandemic.

Intended audience

This manual provides relevant guidance prior to, during and after COVID-19 vaccine introduction for governments, global, regional and national staff from immunization programmes, regulatory authorities, partners and pharmacovigilance centres as well as vaccine manufacturers and marketing authorisation holders.

Organization of the manual

This manual has been developed on the principles described in the Global vaccine safety blueprint[9], the WHO's Global manual on surveillance of adverse events following immunization[10] and the CIOMS guide to active vaccine safety surveillance.[11]

For ease of use the manual has been divided into nine modules (see below) which can be consulted individually. The modules contain hyperlinks to relevant sections of other modules.

Given the rapidly evolving landscape, the modules will be updated as frequently as needed. For this reason, only an electronic version will be made available online, with links to appropriate reference documents and regular updates to incorporate new information and evidence as the COVID-19 vaccines are deployed. Each module will be linked to a slide deck that can be used for training purposes.

Scope of the manual

The modules included in this manual are:

COVID-19 vaccines: description and general safety considerations for implementation

This module outlines the different COVID-19 vaccines that are being developed, their platforms, technologies, development and licensing status, and their unique safety features and potential risks. It

9 WHO. Global vaccine safety blueprint 2.0 (GVSB2.0). Available from: https://www.who.int/vaccine_safety/gvs_blueprint-consultation/en/. Accessed 26 October 2020.

[10] WHO. Global manual on surveillance of adverse events following immunization. Available from: https://www.who.int/vaccine_safety/publications/aefi_surveillance/en/. Accessed 26 October 2020.

[11] CIOMS guide to active vaccine safety surveillance. Available from: https://cioms.ch/publications/product/cioms-guide-to-active-vaccine-safety-surveillance/. Accessed 26 October 2020.

also highlights the safety implications for implementing immunization programmes for priority target populations.

Stakeholders for safety surveillance of COVID-19 vaccines

This module lists the various stakeholders, their roles and responsibilities in COVID-19 vaccine safety surveillance and pharmacovigilance, at the global, regional and national levels. It also provides guidance on how the stakeholders could collaborate to ensure the efficient handling of COVID-19 vaccine safety surveillance and pharmacovigilance.

Establishing COVID-19 vaccine safety surveillance systems

This module provides a list of the minimum requirements that should be in place to effectively monitor and manage COVID-19 vaccine safety issues and the resources required at global, regional and national levels in terms of tools, techniques, technologies and guidance. It defines what is meant by pharmacovigilance preparedness, and provides guidance for the measurement of preparedness, planning and prioritization.

Responding to adverse events following immunization

This module outlines the minimum approaches that countries should have in place for responding to adverse events following COVID-19 immunization also the additional approaches that countries with more resources can undertake. It describes the practical differences for establishing COVID-19 vaccine safety surveillance system based on the types of vaccine platforms, different population profiles, handling high levels of reporting and the need to anticipate new events.

Responding to adverse events of special interest

This module introduces the concept of adverse events of special interest which is a novel entity for many countries and regulatory agencies. It provides guidance on the selection and definition of these events. The need to prepare data on background rates of adverse events of special interest is emphasized.

Data management systems for COVID-19 vaccine safety surveillance

The module describes the different approaches and options available to collect data using the tools available (some of which are still under development), the routing, timelines and the activities to be done at various levels when processing the data and generating information for action. It presents an overview of the approaches undertaken by countries and their efforts to share vaccine safety and pharmacovigilance data. Guidance is provided to show how indicators to measure the functionality of data management systems and the quality of the pharmacovigilance could help programme managers at national, province and district levels.

Engaging with the pharmaceutical industry on COVID-19 vaccine safety

This module describes the essential role played by the private sector, particularly the pharmaceutical industry, in the development and introduction of vaccines, as well as in on-going pharmacovigilance activities to ensure efficacy, quality and safety throughout the vaccines' life cycle. The module will provide guidance on transparent collaboration between the public and private sectors to ensure the safe and effective deployment of COVID-19 vaccines.

Regulatory reliance and work-sharing

This module provides definitions of regulatory reliance and work-sharing and presents some examples of how these approaches have been used. How these approaches could be used for developing COVID-19 vaccine safety surveillance systems, particularly in resource-poor settings, are outlined.

COVID-19 vaccine safety communication

This module provides guidance on communicating about COVID-19 vaccine safety from a programme perspective. It includes a description of factors that influence people's perceptions of vaccine safety; case studies of past experiences with previous pandemics or vaccine safety issues; a synthesis of evidence and recommendations for communication from risk communication; hypothetical scenarios that apply these recommendations to the COVID-19 vaccine context; and criteria for prioritising responses to vaccine safety issues.