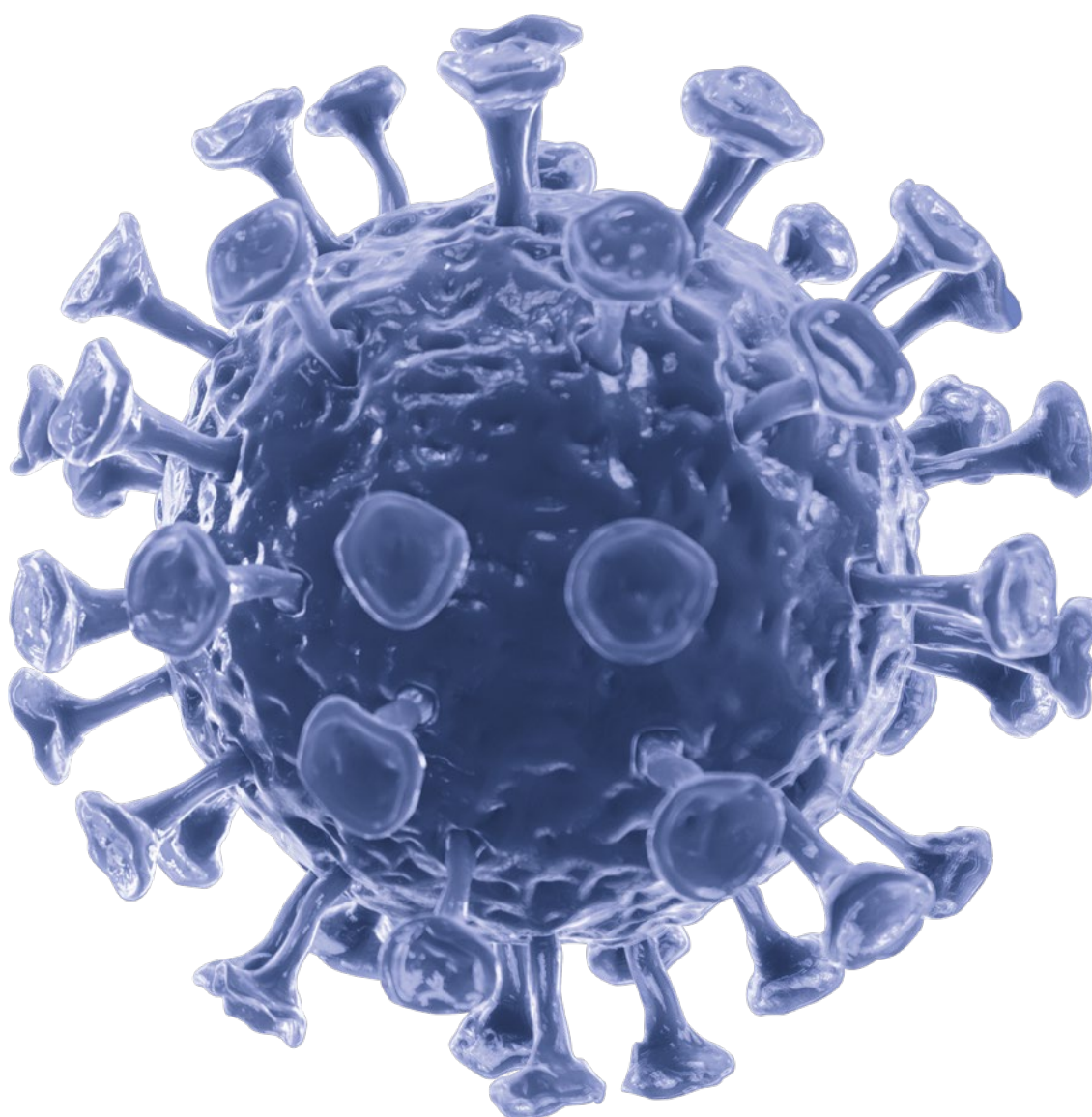


COVID-19 VACCINES:

SAFETY SURVEILLANCE MANUAL

**STAKEHOLDERS IN
COVID-19 VACCINE SAFETY
SURVEILLANCE**

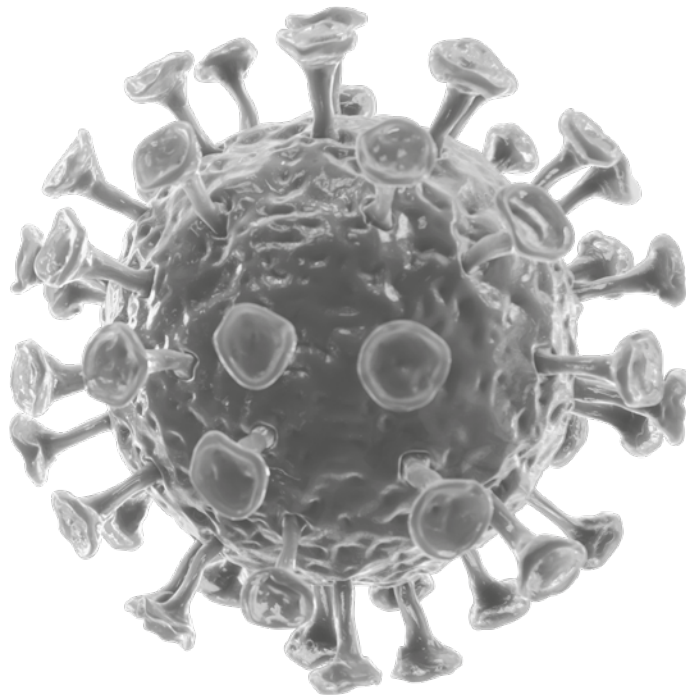


**World Health
Organization**

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SURVEILLANCE
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**World Health
Organization**

Covid-19 vaccines: safety surveillance manual

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Contents

Key points	iv
1. Introduction	1
2. Identification of stakeholders and their roles	2
3. National stakeholders	3
3.1 Ministries of Health	3
3.2 National regulatory authorities	3
3.3 Expanded programmes on immunization and national immunization programmes	4
3.4 National pharmacovigilance centres	5
3.5 AEFI review committees	6
3.6 National immunization technical advisory groups	7
3.7 Vaccine manufacturers	7
3.8 Academia	8
3.9 Health care workers	8
3.10 Beneficiaries	9
3.11 Media	9
3.12 Non-governmental organizations and professional societies	10
4. Regional stakeholders	10
4.1 Regional regulatory networks	10
4.2 Regional technical advisory committees on vaccine safety	10
5. Global stakeholders	11
5.1 International Coalition of Medicines Regulatory Authorities	11
5.2 The Council for International Organizations of Medical Sciences	11
5.3 International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use	12
5.4 WHO prequalification	12
5.5 WHO Global Advisory Committee on Vaccine Safety	13
5.6 WHO Strategic Advisory Group of Experts	13
5.7 WHO Immunization, Vaccines and Biologicals Department	15
5.8 UNICEF	15
5.9 Uppsala Monitoring Centre	15
5.10 Brighton Collaboration	16
5.11 COVID-19 Vaccines Global Access Facility	16
5.12 Vaccine Safety Net	16
5.13 The Coalition for Epidemic Preparedness Innovations	17
5.14 International Federation of Pharmaceutical Manufacturers and Associations	17
5.15 Developing Countries Vaccine Manufacturers Network	17

Key points

- Vaccine safety monitoring requires broad and timely collaboration between national, regional and global stakeholders.
- International collaboration will be essential to verify the safety and effectiveness of the many COVID-19 vaccines that will be produced and used in many different countries and administered to large numbers of people in a short period of time.
- Mapping national, regional and global stakeholders and their responsibilities is key for ensuring appropriate vaccine safety monitoring of the COVID-19 vaccines when they are deployed.
- Stakeholders will continue their regular pharmacovigilance activities and many will have additional activities, particularly during COVID-19 vaccine introduction.

01 Introduction

Vaccine safety monitoring, including effective reporting of adverse events following immunization (AEFIs), investigation and assessment of reported cases and taking necessary actions, requires broad and timely collaboration between national, regional and global stakeholders. These stakeholders include:

- vaccine developers, and manufacturers;¹
- regulatory authorities who initially approve vaccine clinical trial protocols, assess their results and, if shown to be safe and efficacious, grant marketing authorizations, and withdraw marketing authorization if the vaccine is found to be unsafe;
- policy makers who recommend the use of vaccines, and specify the relevant vaccine target groups;
- vaccine providers who deliver vaccines and report possible AEFIs;
- the public health institutes that investigate and assess adverse events; and
- beneficiaries.

International collaboration will be essential to verify the safety and effectiveness of the many COVID-19 vaccines that will be produced and used in many different countries and administered to large numbers of people in a short period of time. Therefore, mapping national, regional and global stakeholders and their responsibilities is key for ensuring appropriate vaccine safety monitoring of these newly developed vaccines.

¹ For the purpose of this document, manufacturer also means marketing authorization holder.

02

Identification of stakeholders and their roles

At the core of this collaboration are the immunization service providers who can be public or private, or both, depending on the organization of the country's health care system. It is possible that the role of country's immunization service providers will be extended to offer COVID-19 vaccines to selected target population groups during COVID-19 vaccination campaigns.

Here we list the main national, regional and global stakeholders and describe their routine roles in vaccination and their roles in safety monitoring and assessment for COVID-19 vaccines. The list of stakeholders is not exhaustive; there are many other stakeholders who provide regional or country-specific pharmacovigilance.

In addition to the stakeholders listed here, if pregnant or lactating women are included as a target group for COVID-19 vaccination, collaboration with the relevant maternal and neonatal-child health programmes should be considered.

National stakeholders

In some countries, these stakeholders are present in autonomous regions.

3.1 Ministries of Health

The routine roles of Ministries of Health (MoHs) are to:

- increase support for national immunization programmes and ensure financial sustainability;
- develop and introduce laws, regulations, and policies that support immunization programmes;
- ensure a secure high-quality supply base of vaccines;
- develop region- and country-specific plans, in collaboration with other regional and national stakeholders, when necessary;
- prioritize and assume full ownership of national immunization programmes; and
- create equity-driven programmes that reach all members of the community.

In the context of COVID-19 vaccine safety monitoring, MoHs are expected to:

- ensure availability of funding for national stakeholders to conduct key activities to strengthen safety monitoring for COVID-19 vaccines;
- establish a national coordination task force or working group consisting of multi-disciplinary and multi-agency representatives to ensure inter-stakeholder coordination and cooperation;
- generate vaccine demand and ensure acceptability;
- establish efficient communication mechanisms about COVID-19 vaccines between regulatory authorities, immunization programmes, Ministry of Education and other authorities, so that the population is informed about vaccine safety issues and can report any concerns; and
- be prepared to respond to rumours and media and community concerns.

3.2 National regulatory authorities

The national regulatory authorities (NRA) are responsible for ensuring that any pharmaceutical product, including vaccines, used within the country is (i) of good quality, (ii) effective, and (iii) safe for the purpose or purposes for which it is proposed.

The core functions of the NRA are:

- marketing authorization activities;
- pharmacovigilance, including surveillance of AEFIs;
- NRA batch release, with a system for batch release of vaccines;

- laboratory access, with use of laboratories when needed;
- market surveillance and control;
- regulatory inspection, with regular inspection of vaccine manufacturers for good manufacturing practices (GMP) compliance; and
- regulatory oversight of clinical trials, with evaluation of clinical performance through authorized clinical trials.

It should be noted that not all NRAs engage in all the listed activities and, instead, may adopt the principles of regulatory reliance and work sharing.

In the context of COVID-19 vaccine safety monitoring, NRAs are expected to:

- oversee preparations for emergency use listing (EUL);
- verify submission and review of risk management plans prior to marketing authorization and making risk-based recommendations for post- authorization safety surveillance;
- oversee communication and information sharing with immunization programmes, pharmacovigilance centres and other key institutions on COVID-19 vaccines safety updates to enhance the NRA's ability to make evidence-based decisions to protect public health;
- have authority to mandate COVID-19 vaccine safety studies by the vaccine manufacturers and importers of vaccines, as required;
- have the independent authority to investigate potential safety signals and assure the continued post-authorization safety of COVID-19 vaccines;
- oversee the monitoring of COVID-19 vaccine safety by reviewing the periodic safety update reports (PSURs) / periodic benefit-risk evaluation reports (PBRERs);
- share safety information generated with national, regional, international decision-makers and vaccine manufacturers.

3.3 Expanded programmes on immunization and national immunization programmes

Their routine roles of expanded programmes on immunization (EPIs) and national immunization programmes (NIPs) are to:

- protect the population against vaccine-preventable diseases (principal role);
- respond with timely information, when public concerns about safety and efficacy of vaccines are raised to sustain public trust in vaccines and vaccination;
- be responsible for safe storage, handling, including maintenance of the cold chain i.e., (continuous refrigeration), delivery and administration of vaccines released by the NRA;
- ensure that health care workers respond to adverse events and report them;
- ensure that sufficient training and capacity is provided so that AEFIs are minimized;
- provide feedback to all levels on the findings of the AEFI investigations and causality assessments;
- provide guidance on monitoring, supervision and training to all stakeholders;

- if there are no pharmacovigilance centres in the country:
 - oversee monitoring, information collection, assessment of serious AEFIs;
 - ensure that causality assessments for AEFIs are conducted as per guidelines; and
 - search for and analyse safety signals.
- provide expert support for field investigations; and
- recommend decisions for vaccination policies.

The roles of the EPIs and NIPs for COVID-19 vaccine safety monitoring, in collaboration with NRAs, are expected to include:

- when recommended, conducting specific active surveillance studies for COVID-19 vaccines, similar to those for other new vaccines i.e., typhoid conjugate, malaria, Ebola, and dengue vaccines, with active surveillance and sentinel sites to identifying signals and establish causality;
- regularly reviewing reports submitted to passive safety surveillance systems to identify rates and unexpected patterns, with special attention to serious outcomes, such as death, disabilities, life-threatening events, and programmatic errors;
- identifying and quantifying public concerns surrounding vaccines through cross-sectional surveys and monitoring of social media;
- developing a national framework to process vaccine safety signals and determine which should be prioritized for more rigorous evaluation and risk assessment;
- measuring and characterizing background rates of medical outcomes that may be temporally associated with COVID-19 vaccines;
- measuring and characterizing other AEFIs identified in active surveillance and sentinel systems; and
- coordinating existing active and sentinel surveillance nationally, regionally and globally to ensure harmonization, avoid duplication, increase power to detect rare events and take advantage of variability in vaccination practices and target population.

3.4 National pharmacovigilance centres

The routine roles for national pharmacovigilance centres, when they exist, include:

- collecting and analysing case reports for AEFIs;
- supporting AEFI committees in performing causality assessment for AEFIs;
- detecting and analysing vaccine safety signals;
- alerting prescribers, vaccine manufacturers and the public if new risks for adverse reactions are observed;
- review risk management plans and oversee implementation for pharmacovigilance centres that are within regulatory agencies; and
- overseeing vaccine safety and risk communication.

The roles of the national pharmacovigilance centres for COVID-19 vaccine safety monitoring are expected to include:

- ensuring timely submission of COVID-19 AEFIs and adverse events of special interest (AESIs) data from EPIs, NIPs and pharmacovigilance centres across the country for data compilation, analysis and signal detection; and
- sharing information with key national stakeholders on COVID-19 vaccine safety and with the global community by uploading the information on the WHO global pharmacovigilance database, *Vigibase*, maintained at Uppsala Monitoring Centre (UMC) in Sweden under the WHO International Drug Monitoring Programme.

3.5 AEFI review committees

The main routine responsibilities of AEFI review committees are to:

- provide guidance for AEFI investigations so that the cause can be determined correctly;
- assess potential causal links between AEFIs and vaccines, using standard procedures;²
- monitor reported AEFI data for potential signals of previously unrecognized vaccine-related adverse events and support further investigations to establish if causality exists;
- make the necessary recommendations to rectify problems, communicate with national stakeholders and other national and international experts, when required.

The terms of reference for the AEFI review committees for COVID-19 vaccine safety monitoring are expected to include:

- assessing potential causal links between AEFIs and AESIs and COVID-19 vaccines;
- monitoring AEFI data for identification of potential signals of previously unidentified COVID-19 vaccine related adverse events;
- reviewing all serious AEFIs presented for expert opinion and arranging further investigation to establish causality, if required;
- communicating with other national and international experts, when required, to establish causality and resolve vaccine quality issues;
- advising NRAs, EPIs and NIPs on COVID-19 vaccines AEFI- and AESI-related issues when requested; and
- advising the Ministry of Health (MoH) on COVID-19 vaccines and Immunization safety-related matters when requested.

The committee should be independent of the NRAs, NIPs/EPIs, MoHs and vaccine manufacturers, and the members should have no conflicts of interest.

2 World Health Organization. Causality assessment of an adverse event following immunization (AEFI) User manual for the revised WHO AEFI causality assessment classification (Second edition). Available from: https://www.who.int/vaccine_safety/publications/gvs_aefi/en/. Accessed 30 October 2020.

3.6 National immunization technical advisory groups

The main routine roles of national immunization technical advisory groups (NITAGs) are to:

- guide national governments and policymakers for the development and implementation of evidence-based, locally-relevant immunization policies and strategies that reflect national priorities;
- support NIPs, EPIs and NRAs and empower them to address issues associated with vaccine quality and safety and the introduction of new vaccines and immunization technologies; and
- help governments, NIPs and EPIs to address public concerns.

The roles of NITAGs (or of a COVID-19 working group within the NITAG) for COVID-19 vaccine safety monitoring are expected to include:

- providing the latest information on different COVID-19 vaccine platforms, risk/benefit analyses, COVID-19 vaccine EUL status, etc.; and
- reviewing the available evidence to be considered for recommendations for COVID-19 vaccine introduction, including the identification of priority target groups for COVID-19 introduction.

3.7 Vaccine manufacturers

The routine roles of the vaccine manufacturers are to:

- continue to develop, produce and supply innovative and high-quality vaccines that meet countries' needs in compliance with international GMP standards;
- support research and vaccine specific training needs for immunization;
- establish risk minimization plans for new vaccines;
- participate in open dialogue with countries and the public sector to ensure sustainable access to current and new vaccines; and
- to continue to innovate manufacturing processes and pricing structures.

The roles of vaccine manufacturers for COVID-19 vaccine safety monitoring are expected to include:

- sharing risk management plans and information on detected signals for COVID-19 vaccines with NRAs;
- conducting phase IV studies on COVID-19 vaccines and submitting periodic safety update reports (PSURs) on a regular basis to help policy decisions; the frequency of PSUR submissions may be increased to bi-monthly/monthly to guide quick corrective actions and decisions;
- responding to national requests to share additional and updated product information and clinical trial data;
- responding to national requests to implement innovative risk minimization measures, for example, peel-off labels on vaccine vials; and

- keeping countries updated on all safety and efficacy findings in other countries, particularly from phase IV studies.

3.8 Academia

The main routine roles of academia are to:

- promote innovation to accelerate the development of new and improved vaccines;
- pursue a multidisciplinary research agenda that focuses on transformational impact and is based on the needs of end users;
- provide pharmacovigilance training through its curriculum;
- embrace new ways of working that speed up and improve dialogue with other researchers, regulators and manufacturers; and
- align actions and increase effectiveness in responding to local and global immunization challenges.

The roles of academia for COVID-19 vaccine safety monitoring are expected to include advising and facilitating research activities concerning COVID-19 vaccines, including sentinel-site based and specific studies related to AESIs.

3.9 Health care workers

The routine roles of health care workers are to:

- provide vaccine and vaccination information and then providing high-quality immunization services;
- identify areas where immunization services could be improved and innovations implemented;
- serve as proactive, credible advocates to promote the value of vaccines and vaccination and recruit other advocates;
- use existing and emerging technologies to improve information delivery and capture, using beneficiaries³, if possible;
- dialogue with communities and the media and use effective communications techniques to convey messages about vaccines; and
- address clinical case management for adverse events.

The roles for health care workers for COVID-19 vaccine safety monitoring are expected to include:

- ensuring staff training on detection, management and reporting of COVID-19 vaccine AEFIs identified through active and passive surveillance;

³ Beneficiaries could be encouraged to report potential adverse events using mobile apps and other software, although this could raise problems of confidentiality of information; during the preparedness stage, this issue should be analysed.

- providing supervision to ensure both serious and non-serious AEFIs are captured and that serious AEFIs are adequately investigated; and
- developing a communication protocol, including the use of a trusted spokesperson, to promptly inform the public about any investigation or rumours.

3.10 Beneficiaries

The roles of beneficiaries are the same in the context of COVID-19 vaccine safety monitoring as for routine vaccine safety monitoring, and include to:

- understand the risk and benefits of vaccines and immunization, viewing this as part of being a responsible citizen;
- play an active role in identifying what they feel is important to help define certain adverse effects, if possible;
- differentiate between genuine and false information and ensure that correct information is communicated, and prevent the circulation of false information;
- demand the right to safe and effective immunization programmes from their leaders and government and hold leaders and government accountable for providing them;
- participate in public-health discussions;
- be involved in key decisions about immunization processes;
- participate and contribute to the immunization delivery process; and
- convey the needs and perspectives of their communities to policymakers.

3.11 Media

The routine roles of the media are to:

- understand the benefits of, and concerns about, immunization in order to accurately report on and effectively promote immunization programmes;
- engage in country, regional and global advocacy beyond the immunization community to ensure vaccines and immunization are understood to be a right for all; and
- use effective communications techniques to convey messages about vaccines and to address safety concerns.

The roles for media for COVID-19 vaccine safety monitoring are expected to include:

- keeping up to date with media releases, press information packages, briefing papers, web materials, talking points disseminated by MoHs on COVID-19 vaccines and vaccination;
- proactively identifying, filtering out and preventing the spread of misinformation;
- participating in media workshops and training sessions to learn about the rationale for COVID-19 vaccine introduction and understand the key messages; and
- ensuring the dissemination of clear, factual messages that have been confirmed by the relevant authorities to the public.

3.12 Non-governmental organizations and professional societies

Non-governmental organizations and professional societies do get involved in the promotion and implementation of routine immunization programmes at both the country and global levels, follow national guidelines and regulations for the design and delivery of immunization programmes that fulfil the duty of accountability to national authorities, contribute to improved evaluation and monitoring systems within countries.

Non-governmental organizations and professional societies should participate in the development and testing of innovative approaches for the delivery of COVID-19 immunization services that reach the most vulnerable people.

04 Regional stakeholders

4.1 Regional regulatory networks

Regional regulatory networks such as the African Vaccine Regulatory Forum ([AVAREF](#)), the South-East Asia Regulatory Network ([SEARN](#)), the European Medicines Agency ([EMA](#)) play an essential role in routine pharmacovigilance. For example, EMA's large [Eudravigilance](#) database is a system for managing and analyzing information on suspected adverse reactions to medicines, including vaccines, that have been authorized or are being studied in clinical trials in the European Economic Area and also those authorized for use outside the European Union, the [Article 58 authorized vaccines](#). These latter include vaccines for protection against a WHO public health priority disease, such as COVID-19. These networks play a key role in implementing regulatory reliance for pharmacovigilance of COVID-19 vaccines as described in the [module on regulatory reliance](#).

4.2 Regional technical advisory committees on vaccine safety

The roles of [regional advisory committees](#) on vaccine safety vary between regions. All WHO regions have established [Regional Immunization Technical Advisory Groups](#) (RITAGs) that play different roles to those played by the NITAGs as they provide recommendations on regional

immunization priorities and strategies in the light of regional epidemiological and social issues to the WHO regional directors as well as the countries in their respective regions.

The roles for RITAGS for COVID-19 vaccine safety monitoring are expected to include rapid, real-time exchange of information and joint assessment of routine safety data, should there be a safety signal.

Global stakeholders

5.1 International Coalition of Medicines Regulatory Authorities

The International Coalition of Medicines Regulatory Authorities ([ICMRA](#)) is a voluntary, executive-level entity of worldwide medicines regulatory authorities set up to provide strategic coordination, advocacy and leadership. ICMRA acts as a forum to support international cooperation among medicines regulatory authorities. The coalition aims to identify ways to better use existing initiatives and resources, develop strategies to address current and emerging challenges in global human medicine regulation, such as the growing complexity of globalized supply chains and provide direction for common activities and areas of work.

ICMRA aims to expedite and streamline the development of COVID-19 vaccines and treatments. In April 2020, [ICMRA members pledged to strengthen global collaborative efforts](#) to align the facilitation of rapid development, approval and global roll-out of safe and effective medicines and vaccines to prevent and treat COVID-19. Collective statements and efforts including describing the key characteristics of clinical trials that are most likely to generate the conclusive evidence needed to enable the accelerated approval of potential treatments and vaccines against COVID-19.

5.2 The Council for International Organizations of Medical Sciences

The Council for International Organizations of Medical Sciences ([CIOMS](#)) is an international, non-governmental, non-profit organization established jointly by WHO and UNESCO in 1949. Its mission is to advance public health through guidance on health research and policy including ethics, medical product development and safety. CIOMS has an official relationship with WHO

and is an associate partner of UNESCO. The [CIOMS pharmacovigilance guidelines](#) have been used as the basis for International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines (see **Section 5.3**). The longest running of the CIOMS Working Groups, since 2002, is dedicated to standardized MedDRA queries (SMQs). This implementation working group has produced the 'Red Books' on the [Development and Rational Use of Standardised MedDRA Queries \(SMQs\)](#), updated in 2016. The [CIOMS Guide to Active Vaccine Safety Surveillance](#), published in 2017 will be used for guidance for COVID-19 vaccine safety monitoring. The 2012 report of the CIOMS WHO working group on the [Definitions and Applications of Terms for Vaccine Pharmacovigilance](#) is used as the reference document for AEFI surveillance and causality assessment.

5.3 International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) brings together regulatory authorities and pharmaceutical industries to discuss scientific and technical aspects of pharmaceuticals and to develop ICH guidelines. Since its inception in 1990, ICH has gradually evolved, to respond to increasingly global developments in the pharmaceutical sector and the ICH guidelines are used by a growing number of regulatory authorities. ICH's mission is to achieve greater harmonization worldwide to ensure that safe, effective and high-quality medicines are developed, registered and maintained in the most resource efficient manner whilst meeting high standards. Since its announcement of organizational changes in October 2015, ICH has grown as an organization and now includes 17 Members and 32 Observers.

The COVID-19 pandemic has prompted an urgent need for a harmonized, standardized approach for coding and reporting COVID-19 infections as a global health issue. ICH has defined E2B⁴ as the international standard for transmitting adverse event reports that includes message standards required for effective transmission of individual case safety reports (ICSR). The ICH M1 Points to Consider Working Group and the medical dictionary for regulatory activities (MedDRA) maintenance and support services organization (MSSO), with the approval of the MedDRA Management Committee, are issuing notifications for MedDRA users regarding existing and new terms for COVID-19 concepts. These notifications are available on the [MedDRA website](#). The latest version 23.1 notifies the addition of new terms to MedDRA.

5.4 WHO prequalification

The WHO prequalification (PQ) team has a major role in assuring the quality of all vaccines that could be purchased by UN agencies. It provides Member States and procurement agencies, such as Gavi, the Vaccine Alliance, the Global Fund and UN organizations like UNICEF,

⁴ E2B(R3) individual case safety report (ICSR) specification and related files. Available from: <https://ich.org/page/e2br3-individual-case-safety-report-icsr-specification-and-related-files>. Accessed 23 November 2020.

with the information required to purchase vaccines matching the specific needs of their programme. The WHO prequalification process for vaccines is a comprehensive assessment that takes place through a standardized procedure aimed at determining whether the product meets requirements for quality, safety and efficacy in immunization programmes. The full prequalification assessment process includes the following components:

- review of the quality, safety and efficacy data,
- review of production process and quality control procedures,
- laboratory testing,⁵ and
- WHO site audit of the manufacturing facilities with the responsible NRA.

Once a vaccine is prequalified and introduced to the market, the WHO PQ team ensures it continues to meet standards by, for example, investigating complaints from the field and reports of AEFIs.

The WHO PQ team is playing this major role for the prequalification of new COVID-19 vaccines and for possible EUL of COVID-19 vaccines.

5.5 WHO Global Advisory Committee on Vaccine Safety

The Global Advisory Committee on Vaccine Safety (GACVS) provides independent, authoritative, scientific advice to WHO on vaccine safety issues of global or regional concern with the potential to affect in the short- or long-term national immunization programmes. This includes providing advice on urgent matters, such as COVID-19 vaccine safety monitoring, as needed.

Issues to be considered by the Committee are jointly decided by the WHO Secretariat and the Committee. More specifically, the role of the GACVS is expected to include:

- rigorous review of the latest knowledge, in all fields ranging from basic sciences to epidemiology, concerning all aspects of vaccine safety of global or regional interest, in close collaboration with all parties involved, including experts from national governments, academia, and industry;
- assessment of causality between COVID-19 vaccines and/or their components and adverse events attributed to them;
- creation of ad hoc task forces, when necessary, with a mandate to commission, monitor and evaluate appropriate methodological and empirical research on any suspected association between specific vaccines/vaccine components and adverse event(s); and
- providing scientific recommendations that are intended to assist WHO, the WHO's Strategic Advisory Group of Experts (SAGE) for vaccines and immunization, national governments

⁵ Quality testing of vaccines is organized by the Laboratory Networks & Services (LNS) team. The WHO LNS team leads the WHO National Control Network for Biologicals who bring together national control laboratories and NRAs of vaccine-producing and vaccine-recipient countries, manufacturer's associations as well as other stakeholders. The Network facilitates access to and availability of prequalified vaccines through reliance on batch release of respective network recipient countries.

and international organizations in formulating policies regarding vaccine safety issues, with particular attention to those problems that affect developing countries.

5.6 WHO Strategic Advisory Group of Experts

SAGE serves as the principal advisory group to WHO for the development of policy related to vaccines and immunization. SAGE is charged with advising WHO on overall global policies and strategies, ranging from vaccine and technology research and development, to delivery of immunization and linkages between immunization and other health interventions. The mandate of SAGE is to provide strategic advice rather than technical input, and it is not restricted to childhood vaccines and immunization but extends to the control of all vaccine-preventable diseases. SAGE advises the WHO Director-General specifically on:

- adequacy of progress towards the achievement of the goals of the Global Immunization Vision and Strategy (GIVS)⁶;
- major issues and challenges to be addressed with respect to achieving the goals of GIVS;
- immunization programme response to current public health priorities;
- major general policies, goals and targets, including those related to vaccine research and development;
- adequacy of WHO's strategic plan and priority activities to achieve the GIVS goals consistent with its mandate and considering the comparative advantages and the respective roles of partner organizations;
- cross-departmental activities and initiatives related to vaccine and immunization technologies and strategies and linkages with other health interventions; and
- engagement of WHO in partnerships that will enhance achievement of global immunization goals.

In the context of COVID-19 vaccine safety monitoring, a WHO SAGE working group has been formed to:

- provide continuous review of the available evidence on the progress of candidate vaccines against COVID-19, and provide regular updates to SAGE;
- provide guidance for the development of prediction models to determine the optimal age groups and target populations for vaccine introduction and guide vaccine introduction for optimal impact, and contribute to updates of target population profiles of COVID-19 vaccines for outbreak and endemic use;
- provide policy advice to SAGE on the accelerated use of COVID-19 vaccines (pre-licensure and post-licensure) to mitigate the public health impact of COVID-19, to possibly curtail the ongoing pandemic, as well as to prevent or reduce the risk of spread of disease in the future; this will include recommendations for early allocation of vaccines when vaccine supplies are still limited; and

⁶ World Health Organization. Global Immunization Vision and Strategy. Available from: <https://www.who.int/immunization/givs/en/>. Accessed 8 December 2020.

- provide guidance to ensure equitable access to vaccination, and guidance on the safety of vaccines when safety data from wider population use become available, in close collaboration with GACVS.

The following COVID-19 documents have been endorsed by WHO SAGE:

- [WHO SAGE Values framework for the allocation and prioritization of COVID-19 vaccination](#); and
- [Roadmap for prioritizing population groups for vaccines against COVID-19](#).

5.7 WHO Immunization, Vaccines and Biologicals Department

The Immunization, Vaccines and Biologicals (IVB) Department is responsible for targeting vaccine-preventable diseases, vaccines, immunization policy and research. IVB is involved in addressing immunization challenges in the context of accelerating urbanization, migration and displacement, conflict and political instability, unaffordability of newer vaccines in middle-income countries, unexpected vaccine supply shortages both locally and globally, and rising vaccine hesitancy. Strategies for the continued vaccine preventable infectious disease outbreaks, and disease elimination goals that have not yet been achieved are being developed and pursued.

In the context of COVID-19 vaccine safety monitoring, guidance on national deployment and vaccination plans for COVID-19 vaccines and checklists for immunization programmes preparing for COVID-19 vaccination programmes are being prepared but are not yet available.

5.8 UNICEF

[UNICEF](#) and its partners support immunization programmes in over 100 countries. Their activities include logistics, monitoring and advocacy for immunization and acting on infodemics, and documenting vaccine coverage through the [WHO/UNICEF Joint Reporting Form](#).

In the context of COVID-19 vaccine safety monitoring, UNICEF will provide support to the immunization programmes in countries for vaccination activities and distribution of COVID-19 vaccines.

5.9 Uppsala Monitoring Centre

The Uppsala Monitoring Centre ([UMC](#)) is a WHO Collaborating Centre, located in Uppsala, Sweden that provides training, guidance and support to countries in the WHO Programme for International Drug Monitoring. They manage [VigiBase](#), WHO's database of individual case safety reports (ICSRs) and the world's largest repository of adverse effects from medicines, including vaccines. Member countries submit reports of suspected adverse drug reactions to the database VigiBase. In 2019 VigiBase contained more than 20 million reports. It is used to [analyse global patterns of suspected harm caused by medicines](#) and vaccines and can also be

used to analyse data at national and regional levels. They have also developed and maintain VigiFlow, a web-based ICSR management system for medicines and vaccines, that is E2B compatible. VigiFlow is available to member countries of WHO Programme for International Drug Monitoring (PIDM) and is currently used by more than 90 countries. UMC also provides VigiBase aggregated safety data for the public via VigiAccess™. In the context of COVID-19 vaccine safety monitoring, UMC will be involved in safety signal detection.

5.10 Brighton Collaboration

The Brighton Collaboration develops case definitions for adverse events and guidelines for investigations and assessment of adverse events in formal pharmacoepidemiological studies. In the context of COVID-19 vaccine safety monitoring, a list of possible AESIs have been developed under contract with CEPI (See **Section 5.13**). Case definitions to be used for investigating possible AESIs including background rates are under development. Study protocols are being developed for background incidence studies and association studies initiated for confirmatory studies should a safety signal arise.

Additionally, The Brighton Collaboration Benefit-Risk Assessment of Vaccines by Technology (BRAVATO) template has been developed. This was originally a standardized template to describe the key considerations for the benefit-risk assessment of viral vector vaccines, which has now been broadened to include templates for each of the other major COVID-19 vaccine platform technologies.

5.11 COVID-19 Vaccines Global Access Facility

GAVI co-leading the COVID-19 Vaccines Global Access (COVAX) facility the vaccines pillar of the Access to COVID-19 Tools (ACT) Accelerator. Gavi's impact draws on the strengths of its core partners, the World Health Organization, UNICEF, the World Bank and the Bill & Melinda Gates Foundation. This is a global risk-sharing mechanism for pooled procurement and equitable access to COVID-19 vaccines when they become available. COVAX aims to end the acute phase of the pandemic by the end of 2021.

5.12 Vaccine Safety Net

The Vaccine Safety Net (VSN)⁷ established by WHO, is a network of a diverse digital information resources (websites), VSN members, located in countries around the world and providing scientifically based information on vaccine safety in various languages. The mission of the VSN is to help internet users find reliable vaccine safety information tailored to their needs. A key player in the project is the GACVS (see **Section 5.5**), who developed three categories of criteria for good information practices - regarding credibility, content and accessibility/design to which sites providing information on vaccine safety should comply. VSN evaluates websites

⁷ World Health Organization. Vaccine Safety Net. Available from: <https://www.vaccinesafetynet.org/>. Accessed 8 December 2020.

for their adherence to these criteria. This will be an invaluable resource for information on COVID-19 vaccines and vaccination for all stakeholders.

5.13 The Coalition for Epidemic Preparedness Innovations

The Coalition for Epidemic Preparedness Innovations ([CEPI](#)) is a global partnership launched in 2017 to develop new vaccines for emerging infectious diseases and bring them through to phase I and II vaccine trials. In the context of COVID-19 vaccine safety monitoring, CEPI has signed contracts with 10 vaccine developers and have established partnerships with 5 clinical sample testing laboratories to create a centralised global network for reliable assessment and comparison of the immune responses generated by COVID-19 vaccine candidates. This approach will ensure uniformity in assessment and informed identification of the most promising vaccine candidates. Through this specific network, up to the limit of programme funding, eligible COVID-19 vaccine developers (both CEPI-funded and non-CEPI funded developers) can use the laboratories, without per-sample charges, to analyse the immune response elicited by their COVID-19 vaccine candidates in preclinical, phase I and phase IIa vaccine trials. CEPI has partnered with the Brighton Collaboration in funding the Safety Platform for Emergency vAccines (SPEAC) project in 2019 through the Task Force for Global Health. SPEAC aims to create capacity and solutions for harmonized safety assessment of CEPI vaccines.

5.14 International Federation of Pharmaceutical Manufacturers and Associations

The International Federation of Pharmaceutical Manufacturers and Associations ([IFPMA](#)) represents the research-based pharmaceutical companies and associations across the globe. In the context of COVID-19 vaccine safety monitoring, IFPMA members, which include the leading innovative biopharmaceutical companies in the vaccine field, are aiming to develop safe and effective COVID-19 vaccines.

5.15 Developing Countries Vaccine Manufactures Network

The members of the Developing Countries Vaccine Manufactures Network ([DCVMN](#)) are vaccine manufacturers from developing countries that aim to provide a consistent and sustainable supply of quality vaccines at an affordable price that are accessible to developing countries. In 2020, DCVMN was an alliance between 41 public and private vaccine manufacturing companies from 14 countries and territories engaged in the supply of vaccines for local and international use.

To provide DCVMN members and the Executive Committee with all the information required to make high-level policy decisions, they have set up a COVID-19 committee whose objective is to assess the evolving situation of the pandemic and to:

- evaluate prime COVID-19 vaccine candidates;
- evaluate technical information (research roadmaps, animal models, clinical trial protocols, formulation (e.g. adjuvant effects) etc.);
- evaluate solutions provided by organizations such as, but not limited to, WHO, CEPI, Gavi, PAHO, UNICEF (e.g., COVID-19 AMC, ACT-accelerator, COVAX Facility);
- develop and support solid bases for statements to support DCVMN dialogue with global stakeholders and in public meetings; and
- assess and share technologies important for COVID-19 vaccine development, through surveys and reports.

COVID-19 VACCINES:

SAFETY SURVEILLANCE MANUAL