Stakeholders in COVID-19 vaccines safety surveillance
Learning objectives

- Identify the roles & responsibilities of the various stakeholders in COVID-19 vaccines safety surveillance at global, regional and national levels
- Describe how the stakeholders can collaborate to ensure the efficient handling of COVID-19 vaccines safety surveillance
Stakeholders in COVID-19 vaccines safety surveillance

National

Regional

Global
National stakeholders

- Media
- Beneficiaries
- Academia
- Manufacturers
- HCW
- EPI
- NRA
- NITAG
- National PV centres
- AEFI Committees
- NGOs
- Ministries of health
- National stakeholders
National stakeholders: Ministries of health (MoH)

- 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 for COVID-19 vaccines between regulatory authorities, immunization programmes, Ministry of Education and other authorities
- Be prepared to respond to rumours and media and community concerns.
### National stakeholders: NRAs

- **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**

- **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.**
**National stakeholders: Immunization program**

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<tr>
<th>Activity</th>
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<tr>
<td>when recommended, conduct specific active surveillance studies for COVID-19 vaccines</td>
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<td>regularly review 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;</td>
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<td>identify and quantify public concerns surrounding vaccines through cross-sectional surveys and monitoring of social media;</td>
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<td>develop a national framework to process vaccine safety signals and determine which should be prioritized for more rigorous evaluation and risk assessment;</td>
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<td>measure and characterize background rates of medical outcomes that may become temporally associated with COVID-19 vaccines;</td>
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<tr>
<td>measure and characterize other AEFIs identified in active surveillance and sentinel systems</td>
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<td>coordinate 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.</td>
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National stakeholders: National pharmacovigilance centers

- ensure 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

- share 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.
National stakeholders 
AEFI review committees

- Assess potential causal links between AEFIs and AESIs and COVID-19 vaccines.
- Monitor AEFI data for identification of potential signals of previously unidentified COVID-19 vaccine related adverse events;
- Review all serious AEFIs presented for expert opinion and arrange further investigation to establish causality, if required;
- Communicate with other national and international experts, when required, to establish causality and resolve vaccine quality issues;
- Advise NRAs, EPIs and NIPs on COVID-19 vaccines AEFI- and AESI-related issues when requested.
- Advise 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.
National stakeholders
National immunization technical advisory groups (NITAGs)

Provide the latest information on different COVID-19 vaccine platforms, risk/benefit analyses, COVID-19 EUL status, etc.

Review the available evidence to be considered for recommendations for COVID-19 vaccine introduction, including the identification of priority target groups for COVID-19 introduction.
### National stakeholders: Vaccine manufacturers

<table>
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<tr>
<td>Share risk management plans and information on detected signals for COVID-19 vaccines with NRAs.</td>
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<td>Conduct phase IV studies on COVID-19 vaccines and submit 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.</td>
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<td>Respond to national requests to implement innovative risk minimisation measures, for example, peel-off labels on vaccine vials;</td>
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<td>Respond to national requests to share additional and updated product information and clinical trial data.</td>
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<td>Keep the countries updated on all safety and efficacy findings in other countries, particularly from phase IV studies.</td>
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National stakeholders: Academia

Advise and facilitate research activities concerning COVID-19 vaccines, including sentinel-site based and specific studies related to AESIs.
National stakeholders: Health care workers


### National stakeholders: Beneficiaries

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<td>🤖</td>
<td>Understand the risk and benefits of vaccines and immunization</td>
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<td>👤🔍</td>
<td>Play an active role in identifying what they feel is important to help define certain adverse effects, if possible</td>
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<td>Differentiate between genuine and false information and ensure that correct information is communicated, and prevent the circulation of false information</td>
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<td>Demand safe and effective immunization programmes as a right from their leaders and government and hold leaders and government accountable for providing them;</td>
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<td>☀️ leased</td>
<td>Participate in public-health discussions and be involved in key decisions about immunization processes</td>
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<td>Participate and contribute to the immunization delivery process</td>
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<td>🗣️</td>
<td>Convey the needs and perspectives of their communities to policymakers.</td>
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National stakeholders: Media

- Keep up to date with media releases, press information packages, briefing papers, web materials, talk points disseminated by MoHs on COVID-19 vaccines and vaccination.

- Proactively identify, filter out and prevent the spread of misinformation;

- Participate in media workshops and training sessions to learn about the rationale for COVID-19 vaccine introduction and understand the key messages.

- Ensure the dissemination of clear, factual messages to the public that have been confirmed by the relevant authorities.
National stakeholders
Non-governmental organizations and professional societies

Participate in the development and testing of innovative approaches for the delivery of COVID-19 immunization services that reach the most vulnerable people
Regional stakeholders

Regional regulatory networks
AVAREF (African Vaccine Regulatory Forum)
SEARN (South-East Asia Regulatory Network)
EMA (European Medicines Agency) and the Article 58 authorized vaccines

Regional technical advisory committees on vaccine safety (RTAGs)
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<th>RTAGS</th>
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<tr>
<td>• AVAREF, SEARN or EMA Play an essential role in routine pharmacovigilance</td>
<td>• EMA’s large Eudravigilance database: system for managing and analyzing information on suspected adverse reactions to medicines, including vaccines, those authorized for use outside the European Union, the Article 58 authorized vaccines (i.e. COVID-19 vaccines)</td>
<td>• Regional technical advisory groups play a key role in rapid, real-time exchange of information and joint assessment of routine safety data, should there be a safety signal.</td>
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Global stakeholders
International Coalition of Medicines Regulatory Authorities (ICMRA)

ICMRA aims to expedite and streamline the development of COVID-19 vaccines and treatments

In April 2020, ICMRA members are committed 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
Global stakeholders

The Council for International Organizations of Medical Sciences (CIOMS)

The 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.

The CIOMS guide to active vaccine safety surveillance published in 2017 will be used for guidance for COVID-19 vaccine safety monitoring.
Global stakeholders: International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)

Urgent need for a harmonized, standardized approach for coding and reporting COVID-19 infections as a global health issue

Brings together regulatory authorities and pharmaceutical industries to discuss scientific and technical aspects of pharmaceuticals and develop ICH guidelines

ICH M1 Points to Consider Working Group and the medical dictionary for regulatory activities (MedDRA) maintenance as well as support services organization (MSSO) are issuing notifications for MedDRA users regarding existing and new terms for COVID-19 concepts
Global stakeholders: WHO prequalification

- Major role to assure the quality of all vaccines that could be purchased by UN agencies

- Important role of WHO Prequalification team for the prequalification of new COVID-19 vaccines and for possible EUL of COVID-19 vaccines.

- Review of the quality, safety and efficacy data
- Review of production process and quality control procedures
- Review of production process and quality control procedures
- Laboratory testing, and
- WHO site audit to manufacturing facilities with the responsible NRA
Global stakeholders
WHO Global Advisory Committee on Vaccine Safety (GACVS)

Provides advice on urgent matters as needed, such as COVID-19 vaccine safety monitoring

- The 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
Global stakeholders: WHO Strategic advisory group of experts (SAGE) 1/3

- Provides continuous review of the available evidence on the progress of candidate vaccines against COVID-19

The SAGE serves as the principal advisory group to WHO for the development of policy related to vaccines and immunization.
Global stakeholders: WHO Strategic advisory group of experts (SAGE) 2/3

Provides 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, including recommendations for early allocation of vaccines when vaccine supplies are still limited.

Provides 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.
Global stakeholders: WHO Strategic advisory group of experts (SAGE) 3/3

WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination, 14 Sep 2020

Roadmap for prioritizing population groups for vaccines against covid-19, 27 Sep 2020
Global stakeholders: WHO Immunization, Vaccines and Biologicals Department (IVB)

Provides guidance on national deployment and vaccination plans for COVID-19 vaccines and checklists for immunization programmes preparing for COVID-19 vaccination programmes

The IVB is responsible for targeting vaccine-preventable diseases, vaccines, immunization policy and research
Global stakeholders: UNICEF

UNICEF is expected to provide support to the immunization programmes in countries for vaccination activities and distribution of COVID-19 vaccines.

UNICEF Main activities include logistics, monitoring and advocacy for immunization and acting on infodemics, and documenting vaccine coverage through the WHO/UNICEF Join reporting form.
Global stakeholders: Uppsala Monitoring Center (UMC)

UMC is expected to be involved in safety signal detection

- **UMC Provides training, guidance and support to countries in the WHO Programme for International Drug Monitoring**
Global stakeholders: Brighton collaboration

Specific list of possible AESIs has been developed under contract with Coalition for epidemic preparedness Innovations (CEPI).

Case definitions to be used for investigating possible AESIs including background rates are under development as well as Study protocols for background incidence studies and association studies initiated for confirmatory studies should a safety signal arise.

Templates for each of the other major COVID 19 vaccine platform technologies developed (BRAVATO)

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**BRAVATO (ex-V3SWG)**

Benefit-Risk Assessment of VAccines by TechnoloGY (BRAVATO; ex-V3SWG)

In recognition of the increasing importance of viral vectors for the development of new vaccines and the need to understand their associated safety issues, the Brighton Collaboration (BC) created the Viral Vector Vaccines Safety Working Group (V3SWG) in October 2008. V3SWG was renamed to Benefit-Risk Assessment of VAccines by TechnoloGY (BRAVATO) in July of 2020, so as to expand beyond just vaccines using viral vectors. BRAVATO has two major activities:

1. Developing harmonized guidelines for assessing/addressing potential safety issues of concern for vaccines as listed in Table 1 of this paper, and initially identified in the meeting report from a World Health Organization Informal Consultation on Characterization and Quality Aspects of Vaccines Based on Live Viral Vectors, WHO HQ, Geneva, 4-5 December, 2003.

2. Completing standardized templates with key considerations for a risk/benefit assessment on new vaccine candidates to: a) facilitate scientific discourse among key stakeholders by increasing the transparency and comparability of information; and b) provide a checklist like tool for managing potential complex risks.
Global stakeholders
COVID-19 Vaccines Global Access Facility (COVAX)

A global risk-sharing mechanism for pooled procurement and equitable access to COVID-19 vaccines when they become available.

Aims to end the acute phase of the pandemic by the end of 2021
Global stakeholders
Vaccine safety net

Invaluable resource for information on COVID-19 vaccines and vaccination for all stakeholders.

Websites’ adherence evaluation

Network of a diverse group of digital information resources (websites and social media), VSN members, located in countries around the world and providing scientifically based information on vaccine safety in various languages.
Global stakeholders

The Coalition for Epidemic Preparedness Innovations (CEPI)

- **Global partnership launched in 2017 to develop new vaccines for emerging infectious diseases and bring them through to phase I and II vaccine trials**
- **Contracts signatures with 10 vaccine developers**
- **Partnerships with 5 clinical sample testing laboratories to create a centralised global network to reliably assess and compare the immunological responses generated by COVID-19 vaccine candidates**
- **Uniformity in assessment and informed identification of the most promising vaccine candidates**
- **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**
Global stakeholders
International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)

The IFPMA represents the leading innovative biopharmaceutical companies in the vaccine field

Aim is to develop safe and effective COVID-19 vaccines
Global stakeholders
Developing Countries Vaccine Manufactures Network (DCVMN)

Aim: to provide a consistent and sustainable supply of quality vaccines at an affordable price that are accessible to developing countries

share technologies important for COVID-19 vaccine development, through surveys and reports.

DCVMN is an alliance of over 40 public and private vaccine manufacturing companies from 14 emerging countries/territories engaged in supply of vaccines for local and international use.
Global stakeholders: Role of the COVID-19 committee of the Developing Countries Vaccine Manufactures Network (DCVMN)

- 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

- Assess and share technologies important for COVID-19 vaccine development, through surveys and reports.
Key points to remember...

- 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 broadly used.

- Stakeholders will continue their regular pharmacovigilance activities and many will have additional activities, particularly during COVID-19 vaccine introduction.

- 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.
References


• WHO SAGE Values framework for the allocation and prioritization of COVID-19 vaccination: https://apps.who.int/iris/handle/10665/334299

• Roadmap for prioritizing population groups for vaccines against COVID-19: https://www.who.int/immunization/sage/meetings/2020/october/Session03_Roadmap_Prioritization_Covid-19_vaccine.pdf?ua=1

• Access to COVID-19 tools (ACT) accelerator: https://www.who.int/initiatives/act-accelerator/

• The Brighton Collaboration Benefit-Risk Assessment of Vaccines by Technology (BRAVATO) templates: https://brightoncollaboration.us/category/pubs-tools/templates/

• The Vaccine Safety Net: https://www.vaccinesafetynet.org/