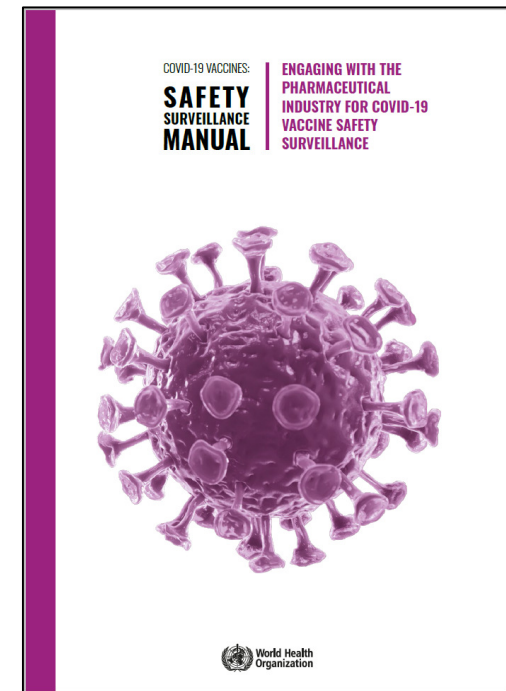
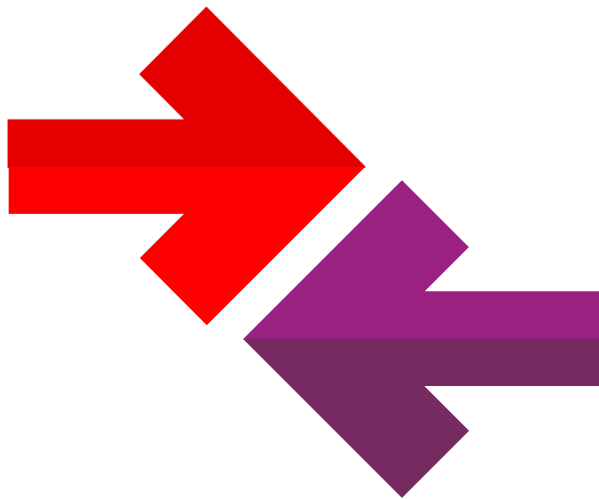


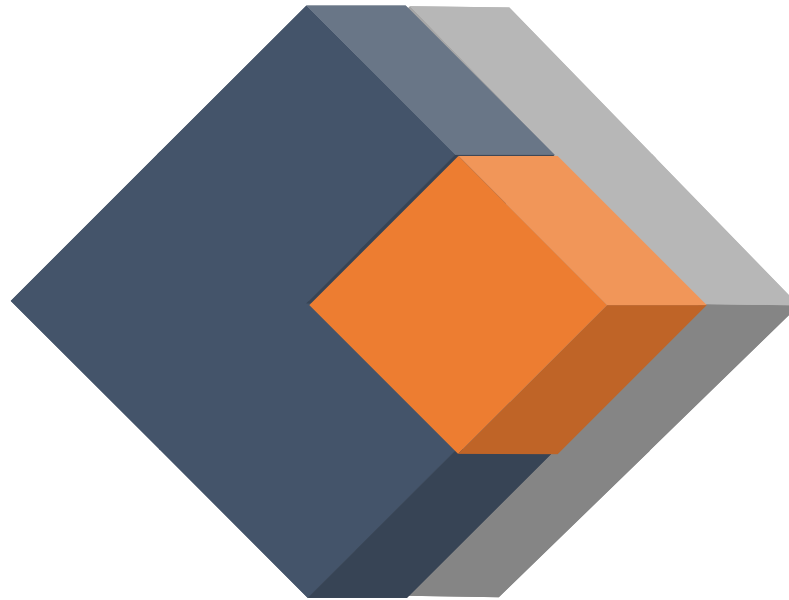
Engaging with the Pharmaceutical Industry for COVID-19 vaccine safety surveillance



Introduction and purpose of module

Pharmaceutical industry

- plays a critical role in the accelerated development of vaccines and therapeutics
- has an essential role in verifying the safety of COVID-19 vaccines through vaccine safety surveillance activities described in risk management plans



This module highlights the role of the pharmaceutical industry in monitoring the safety of COVID-19 and provides a strategy of how NRAs in LMICs can obtain, engage and review safety information provided by market authorization holders.

Objectives and expected outcomes



To describe the role of the Pharmaceutical industry in the safety monitoring of COVID-19 Vaccines

List core components of the risk minimization plan (RMP), understand when a regional annex is needed and what it contains

Explain changes in routine PV plan of RMP required for COVID-19 vaccines

List additional activities in the RMP required for COVID-19 vaccines

Explain the roles of stakeholders that oversee pharmaceutical industry activities at national, regional and global level

Understand how to encourage data sharing in countries that do not mandate data sharing

Know training needs of different target groups on RMP assessment, post authorization studies and implementation of risk minimization plans. Map what bodies/institutions are available to train different target groups

Content



Legal provisions and guidelines



Data Sharing



Risk Management Plans



Training



Oversight



Funding

1. Legal Provisions and guidelines

ICH1 countries	Non ICH countries
<ul style="list-style-type: none">• ICH technical guidelines for Covid-19 vaccine registration and continued monitoring of safety:<ul style="list-style-type: none">• ICH E2E Pharmacovigilance planning• ICH E2C Periodic benefit-risk evaluation report (PBRER)	<ul style="list-style-type: none">• Existing legislation:<ul style="list-style-type: none">• Interpreted to Covid-19 pandemic situation, to provide clear guidance to marketing authorization holders

1 ICH:International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

Members: Europe, USA, Japan, Canada, Switzerland, Brazil, Singapore, Republic of Korea, China, Turkey, Chinese Taipei

Observers: Argentina, India, Cuba, Mexico, Israel, Colombia, Jordan, Moldova, Lebanon, Kazakhstan, Malaysia, Iran, Russia, South Africa, Armenia, Saudi Arabia and Australia

2. Risk Management Plans



Contract between MAH and NRA

Summarizes the safety profile of a medicinal product and lists further studies that will be carried out post-authorisation as well as any extra risk minimisation measures required to be put in place to manage the identified risks of the medicinal product



Submitted in the market authorization dossier



Provides key information on plans for studies and activities to address gaps in knowledge about the safety profile



Provides plans for risk minimization



RMP is an evolving document as more information becomes available, and as we learn more about the profile of AEs from safety studies and benefit risk balance

2. Risk Management Plans



Format and components of RMPs



Routine pharmacovigilance plan



Additional PV activities



Specific considerations under two different scenarios

2. Risk Management Plans for Covid-19 vaccines

Format and components



MAH encouraged to adopt existing formats e.g. EU RMP or use global or core RMPs



All RMPs should contain the following components:

- Safety specification
- Pharmacovigilance activities
- Risk minimization activities
- Evaluation of risk minimization measures

2. Risk Management Plans for Covid-19 vaccines

Format and components



Regional specific annex should be included (takes into consideration additional context specific to the region), e.g. epidemiological characteristics, medical practice, ethnicity, limitations of logistics and regional health and regulatory systems



Regional annex for Covid-19 vaccines should:

- Highlight differences in safety concerns between regions where the vaccine is being launched (e.g. differences in frequency, severity or nature of safety concerns)
- Confirm that the PV and risk minimization activities are compatible with specific safety concerns

2. Risk Management Plans

Routine pharmacovigilance plan the vaccine manufacturer or MAH should describe in the RMP



Specific activities for collection, compilation, assessment and reporting of AEFI to NRA



Format, content and periodicity of PSURs/PBRERs

Usual 6 month reporting cycle too long, as there is expected high levels of exposure within a short period of time

In addition to 6 month PSUR/PBRER, a monthly safety summary focusing on AEDI should be submitted or more frequently as the situation requires



Other requirements defined in the regional annex

Challenges such as large volume of reports of adverse events following immunization (AEFIs) associated with a mass vaccination campaign should be considered and reflected in the planning document.

2. Risk Management Plans

Monthly safety summaries



Include a summary of vaccine distribution (number doses, locality of distribution)



Global numbers (with country of origin) and analysis of AEsIs reported in individuals following immunization, following the Brighton Collaboration recommendations for COVID-19 vaccines



Numbers of deaths and relevant case histories, including observed over expected analysis

2. Risk Management Plans

Additional pharmacovigilance activities



PASSs should be considered and reflected in RMP if planned clinical trials and routine activities do not provide enough information for the complete characterization of important identified and potential risks.



The pharmacovigilance plan will stop when national competent authorities decide it is no longer needed

2. Risk Management Plans

Scenario 1: Covid-19 vaccines submitted for WHO Prequalification Emergency Use Listing - For vaccines introduced in countries outside of country originally authorized, that may not have the resources to implement RMP:



MAH could be required to include additional considerations and PV activities in country where vaccine will be introduced, and if possible a regional annex is preferred.



Details of monthly safety summaries and PASS will be agreed as part of WHO PQ/EUL procedure



Vaccine manufacturer will be responsible for compiling and submitting monthly safety and PSURS/PBRERS to local competent authority



Planned PASS should be carried out by vaccine manufacturers or its local representatives



Multi-country collaborative PASS more ideal; with PASS implemented in selected sites based on capacity and previous experience

2. Risk Management Plans

Scenario 2: Covid-19 vaccines not submitted for WHO Prequalification Emergency Use Listing



This may include smaller companies that implement COVID-19 vaccines in LMICs.



Vaccine may not have undergone stringent review for authorization by a regulatory authority and MAH may have limited resources and only limited PV systems in place.



Smaller MAHs should consider collaborating with other MAHs, to prepare a common RMP for the region where the vaccine will be introduced.

2. Risk Management Plans

Scenario 2: Covid-19 vaccines not submitted for WHO Prequalification Emergency Use Listing



Wherever feasible, regional cooperation and coordination should be adopted; this can include::

- Joint regional review of RMPs through regulatory reliance or task-sharing with an oversight of a regional review committee, E.g. African Vaccine Regulatory Forum (AVAREF), Western Pacific Regional Alliance of NRAS (WPRA), Pan American Network for Drug Regulatory Harmonization (PANDRH)



Multi country safety studies



Training should be provided to smaller MAHs on:

- Core RMP components
- Regulatory obligations for vaccine PV for the region

3. Oversight

National level (NRA)

NRA responsible for:

- Clear guidance and requirements for PV
- Contribute to regional annex for RMP to establish criteria for study site selection
- Provide oversight for study implementation
- Guidance to MAH on requirements for routine communication of study findings, adhoc communications for urgent emerging issues
- Implement a coordinated routine communication plan with stakeholders
- Ensure a national committee is ready to review any national PASS data

Regional (Regional review committee)

- Participate in WHO PQ assessments of RMP for COVID-19 vaccines (providing a regional prospective)
- Advise when a regional annex to the RMP would be justified
- Develop and communicate clear guidance to MAH on criteria for study site selection in region
- Review results from multi-country collaborative PASS in the region

International (International Review committee)

- Review the study protocols for PASS
- Review and analyse multi-country study data
- Provide support to WHO PQ team for analyses of RMPs and PSURS/PBRERs

4. Data Sharing

Effective data flow needed between NRA and the WHO global database of Individual Case Safety Reports (VigiBase); and between NRA and vaccine manufacturer.

NRAs should consider making data sharing a condition of marketing authorization, or a data sharing agreement or memorandum of understanding could be established between the vaccine manufacturer and the NRA.



Data sharing platform needed to:

- Enable data pooling from multi-country sites
- Enable review committees to review PLSS outcomes
- Identify patterns of safety issues of regional importance

Close collaboration between national stakeholders such as NRA and EPI or NIP is critical

WHO PQ programme should consider making data sharing a condition of inclusion of a vaccine on the EUL.

5. Training



Training on legislations for PV, RMPs, safety studies review and PV for vaccine safety is needed for NRA, national and regional committees and MAH.



It is critical that there is a designated QPPV who can set up in-country PV systems



Networks that can help coordinate and deliver training to private sector:

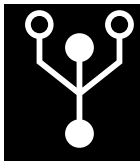
- DCVMN (Developing 255 Countries Vaccine Manufacturers Network)
- IFPMA (International Federation of Pharmaceutical 256 Manufacturers and Associations)

5. Training

Training needs	Training Target				Training providers
	NRA/PV review staff	National AEFI Committee	Regional Review Committee	MAH / subsidiary	
Legislation and legal obligations for pharmacovigilance	✓			✓	DCVMN, IFPMA, ISoP, NRA
RMP review: common core elements, regional annex, iS-PSUR core elements	✓		✓		WHO, NRA
Ethics review of study protocols	✓	✓	✓		CIOMS, WHO
Review of safety study outcomes		✓	✓		WHO, GACVS, AACVS
Pharmacovigilance for vaccine safety	(✓)			✓ *	DCVMN, IFPMA

** Qualified person responsible for pharmacovigilance (QPPV)*
AACVS: African Advisory Committee on Vaccine Safety;
CIOMS: Council for International Organizations of Medical Sciences;
DCVMN: Developing Countries Vaccine Manufacturers Network;
GACVS: Global Advisory Committee on Vaccine Safety;
IFPMA: International Federation of Pharmaceutical Manufacturers and Associations;
ISoP: International Society of Pharmacovigilance;
NRA: national regulatory authority;
WHO: World Health Organization

6. Funding



Post-licensure safety studies

COVAX , the vaccine
pillar of the ACT
Accelerator can support
studies conducted by
MAH



Training

- NRAs Co-funded by several stakeholders (e.g. GAVI Vaccine alliance, WHO, using technical expertise from stringent regulatory agencies)
- MAHs - Industry networks (DCVMN, IFPMA)

Summary of Key Concepts

The pharmaceutical industry has an essential role in verifying the safety of COVID-19 vaccines through vaccine safety surveillance activities described in risk management plans for licensed vaccines particularly via periodic safety update reports

Effective data flow should be established between NRAs or the WHO prequalification team and the vaccine manufacturer while respecting data security and patient privacy

Training to enhance pharmacovigilance competencies and to enable regional coordination should be coordinated and existing training materials and programmes should be leveraged as much as possible



National regulatory agencies (NRAs) and the WHO prequalification team should consider making data sharing a condition of marketing authorization or prequalification for COVID-19 vaccines during the pandemic, particularly in countries

Vaccine manufacturers are encouraged to adopt existing formats for risk management plans, which contain essential elements, such as a safety specification section, pharmacovigilance activities, risk minimization activities, and evaluation of the effectiveness of the risk minimization measures

Quiz

- What should be provided to complement PSURs for COVID-19 vaccines and how often ?
- What should be included in the regional annex of a RMP?
- What is the role of the international review committee in terms of oversight?
- In countries where data sharing between vaccine manufacturer and NRA is not a mandate what can be put in place?