The global smart pharmacovigilance strategy

World Health Organization

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Contents

Message from the Assistant Director-General, Health Systems, Access and Data

Nobody should be harmed when seeking care. Our collective efforts to strengthen health systems must include effective measures to ensure the safety of medicines and other health technologies. This is especially important in the current context of multiple complex challenges, limited resources, and competing priorities.

This document, *The global smart pharmacovigilance strategy,* provides evidence-based information to support Member States to address their most pressing health care needs while building robust, resilient and lasting pharmacovigilance systems. It complements the WHO Programme for International Drug Monitoring.

Drawing on products and programmes such as these, all of us have a role to play – from patients and their families to health care professionals, regulatory agencies and more.

Working together, we can help ensure that everyone, everywhere can access the safe and effective medicines and health products that they need – and accelerate progress towards health for all.

Dr Yukiko Nakatani

Assistant Director-General
Health Systems, Access and Data Division
World Health Organization

Foreword

Trust in regulated medical products (medicines, vaccines and other health products) to protect health, is mostly based on a number of principles: the evaluation before marketing authorization, the permanent oversight of manufacturing facilities and a permanent assessment of benefit/risk balance all through the products life cycle.

Science is at the forefront of this ecosystem, and the transparency of regulatory procedures plays an essential role in building the much needed societal trust.

Behind every product lies a system that must safeguard not only its quality and effectiveness but also its safety. Too often, pharmacovigilance and broader regulatory functions are fragmented, underfunded or disconnected from the wider health infrastructure, leaving millions – particularly in low- and middle-income countries – exposed to avoidable risks. The COVID-19 pandemic served as a global stress test, brutally exposing these vulnerabilities and underscoring the urgent need for resilient, reliable, agile and responsible regulatory systems.

The present *The global smart pharmacovigilance strategy* was developed in response to these challenges. It is built on a simple but powerful idea: safety systems do not need to be complex to be effective – they need to be designed intelligently, to build pharmacovigilance systems that are not only functional but also strategic, sustainable, and tailored to national priorities. It is not a rigid checklist, but a practical framework to help countries prioritize, build capacity, and embed sustainable pharmacovigilance into regulatory systems as well as broader health systems shaped by real-world experience.

The vision is clear: to foster pharmacovigilance and regulatory systems that are strong, adaptive and trusted – systems that guarantee equitable access to affordable, quality-assured health products for everyone everywhere. This is not only a technical priority but also an ethical imperative, especially as disparities in access to essential health products persist and global health challenges evolve.

From the recommendations at the 2018 International Conference of Drug Regulatory Authorities (ICDRA) in Dublin (Ireland) up to today, successive forums have set the sense of urgency for the proposed improvements.

The global smart pharmacovigilance strategy represents a comprehensive alignment, moving the existing recommendations under an adaptive framework that establishes a risk-based prioritization, meeting the need to address innovation and also to implement reliance mechanisms, within global multilateral cooperation mechanisms.

More than an incremental change, the strategy focuses on the centrality of risk management in a global system, building on multilateral cooperation, collectively owned by regulators and stakeholders.

With science and evidence data as the main driving forces, it brings a new hope for collective global action, supported by science, in a permanent combat against misinformation.

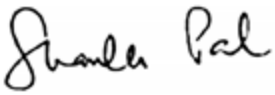
As this strategy is launched, we reaffirm our commitment to the overarching vision of WHO's 14th General Programme of Work: to promote, provide and protect the health and well-being of all people, everywhere. Together, with the strategic action plan of the WHO Regulation and Prequalification programme, the strategy represents a decisive step in strengthening global regulatory systems through enhanced pharmacovigilance.

Dr Rogério Paulo Pinto de Sá Gaspar

Director, Regulation and Prequalification Department
World Health Organization

To our partners

Building on decades of global experience, including the WHO Programme for International Drug Monitoring and the Global Vaccine Safety Initiative, *The global smart pharmacovigilance strategy* provides a framework for building systems that are resilient, responsive and sustainable. We are deeply grateful to our dedicated teams, partners and stakeholders worldwide for their commitment and collaboration. Together, we are forging a future where safe, effective, quality assured and affordable health products are not a privilege, but a shared global public good. Thank you for your support as we advance this critical goal of global smart pharmacovigilance.



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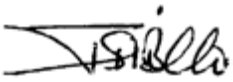

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Stakeholder consultation

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Abbreviations

3S	Smart Safety Surveillance
ADR	adverse drug reaction
AE	adverse event
AEFI	adverse event following immunization
AESI	adverse event of special interest
AMRH	African Medicines Regulatory Harmonization
CIP	Coalition of Interested Parties
EMA	European Medicines Agency
EU	European Union
GVDN	Global Vaccine Data Network
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
HIC	high-income country
ICSR	individual case safety report
IDP	institutional development plan
ISOP	International Society of Pharmacovigilance
LMIC	low- and middle-income countries
NRA	national regulatory agency
PMDA	Pharmaceuticals and Medical Devices Agency
PV	pharmacovigilance
RMP	risk management plan
SEARN	South East Asia Regulatory Network
SPEAC	Safety Platform for Emergency Vaccines
UMC	Uppsala Monitoring Centre
US FDA	United States Food and Drug Administration
VSN	Vaccine Safety Net
WLA	WHO Listed Authority

Glossary

Adverse event (AE). Any untoward medical occurrence that may present during treatment with a medicine or vaccine, but which does not necessarily have a causal relationship.

Adverse event of special interest (AESI). A pre-specified, medically-significant event that has the potential to be causally associated with a medicine or vaccine that needs to be carefully monitored and confirmed by further special studies.

Adverse drug reaction (ADR). A response to a medicine that is noxious and unintended, and which occurs at doses normally used in humans.

Adverse event following immunization (AEFI). Any untoward medical event that follows immunization and that does not necessarily have a causal relationship with the use of the vaccine. It may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.

Conditional marketing authorization. The approval (with conditions) of medicines and vaccines that address unmet medical needs of patients based on less comprehensive data than normally required. The available data must indicate that benefits outweigh risks, and the applicant should be able to provide comprehensive clinical data in the future. This is also referred to as conditional approval.

Emergency use authorization. A mechanism used by regulatory authorities to expedite the availability of unlicensed medical products, including medicines and vaccines, during a public health emergency. This also includes unapproved uses of approved medical products, for example in a new indication.

International standards and guidelines. For the purpose of this document, the term includes relevant internationally recognized standards (e.g. International Organization for Standardization or pharmacopoeial standards) and guidelines (e.g. International Council on Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) or guidelines of the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme).

Marketing authorization. A procedure for approval of a medical product for marketing after it has undergone a process of evaluation to determine the safety, efficacy and quality of the product and the appropriateness of the product information. Once a national regulatory agency (NRA) issues a marketing authorization for a new vaccine, for example, the vaccine may be marketed and/or made available for health care professionals. Also referred to as 'licensing' or 'registration'.

Pandemic. A pandemic (or global epidemic) occurs when a pathogen, typically a virus that is significantly different from circulating viruses and against which almost no one is immune, appears and spreads over several countries or continents, usually affecting many people. The Director-General of the World Health Organization (WHO) may, as

appropriate, declare a public health emergency of international concern under the International Health Regulations (2005) following the identification and determination of the global spread of the disease. Six events were declared public health emergencies of international concern between 2007 and 2020: 2009 H1N1 influenza pandemic; Ebola (West African outbreak 2013–2015, outbreak in Democratic Republic of Congo 2018–2020); poliomyelitis (2014 to present); Zika (2016), COVID-19 (2020 to present); and Mpox (2024).

Recognition. Acceptance of the regulatory decision of a regulator or trusted institution. Recognition should be based on evidence that the regulatory requirements of the reference regulatory authority are sufficient to meet the regulatory requirements of the relying authority. Recognition may be unilateral or mutual and may, in the latter case, be the subject of a mutual recognition agreement.

Reference regulatory authority. For this document, a national or regional authority or a trusted institution such as the WHO Prequalification Programme (WHO/PQ) whose regulatory decisions and/or regulatory work products are relied upon by another regulatory authority to inform its own regulatory decisions.

Regional regulatory system. A system of individual regulatory authorities, or a regional body composed of individual regulatory authorities, operating under a common regulatory framework, but not necessarily under a common legal framework. The common framework must at least ensure equivalence among the members in terms of regulatory requirements, practices and quality assurance policies. The system or regional body may have enforcement powers to ensure compliance with the common regulatory framework.

Reliance. The act whereby a regulatory authority in one jurisdiction takes into account and gives significant weight to assessments performed by another regulatory authority or trusted institution, or to any other authoritative information, in reaching its own decision. The relying authority remains independent, responsible and accountable for the decisions taken, even when it relies on the decisions, assessments and information of others.

Risk management plan (RMP). A document established by the medicine or vaccine manufacturer that contains the following elements: (a) identification or characterization of the safety profile of the medical product(s) concerned; (b) indication of how to characterize the safety profile of the medical product(s) concerned further; (c) documentation of measures to prevent or minimize the risks associated with the medical product, including an assessment of the effectiveness of those interventions; (d) documentation of post-authorization obligations that have been imposed as a condition of marketing authorization.

Work-sharing. A process by which NRAs of two or more jurisdictions share activities to accomplish a specific regulatory task. Work-sharing also entails exchange of information consistent with the provisions of existing agreements and compliant with each agency or institution legislative framework for sharing such information with other NRAs.

VigiBase. A WHO global database of individual case safety reports (ICSRs) including ADRs and AEFIs, maintained by Uppsala Monitoring Centre.

VigiFlow. A web-based ICSR management system (ICH E2B compatible) for medicines and vaccines, developed and maintained by Uppsala Monitoring Centre.

VigiMobile. Developed for field reporting of suspected adverse events for medicines and vaccines. Health workers can use the online/offline forms to collect adverse event data any time, in any setting and on any device. Once online, the system sends reports directly to VigiFlow or a national data management database for further investigation.

VigiLyze. A signal detection and signal management tool that draws on insights into the safer use of medicines from members of the WHO Programme for International Drug Monitoring as a starting point for efficient quantitative signal detection. It supports national signal management processes, including qualitative assessments.

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(All references were accessed on 2 June 2025).

Executive summary

The *global smart pharmacovigilance strategy* guides countries in building and strengthening pharmacovigilance (PV) systems, ensuring the safety of medicines and vaccines in Member States. It is intended as a reference document for national regulatory agencies, expanded programmes on immunization and PV partners in countries, and builds on the concepts of the *Global vaccine safety blueprint* and the Smart Safety Surveillance (3S) pilot projects. The strategy focuses on four aspects that countries need to consider when building or strengthening their PV systems:

1. **Previous efforts, lessons learnt and existing PV resources**. Pharmacovigilance has advanced significantly since the launch of the WHO Programme for International Drug Monitoring in 1968. It is essential to build on the achievements of Member States, WHO and other stakeholders. These include: the development of standardized reporting processes, dictionaries and case definitions; the establishment of infrastructure and resources for training and capacity building; recognition of the value of patient reporting and complementary PV methods; the creation of data management tools and emphasis on interoperability; efforts to address language barriers; attention to safety information for special populations; region-specific initiatives; and the integration of PV into public health and immunization programmes.

2. **Risk-based approach and prioritization**. In the context of limited resources, countries are encouraged to prioritize their PV efforts by focusing on: products of specific relevance to their settings (e.g. medicines for endemic conditions); safety data that are unlikely to be generated elsewhere; and active participation in global PV efforts for new products introduced simultaneously across high-, middle-, and low-income countries.

3. **Work-sharing and reliance**. The overarching vision of the WHO *14th General Programme of Work* (GPW14) is to promote, provide and protect the health and well-being of all people, everywhere. *The global smart pharmacovigilance strategy* acknowledges the wide variation in health system capacity across Member States – ranging from fragile to more mature systems. It encourages countries to prioritize PV activities based on their available resources and regulatory capacity, and to tailor development plans accordingly. The principles of work-sharing and reliance are central to enabling this flexible, context-specific approach.

4. **Anchoring PV in the overall regulatory system-strengthening efforts**. For PV to be sustainable, it must be integrated into the overall regulatory framework. Robust legal provisions empower regulatory authorities to implement and oversee safety monitoring effectively. The *WHO Global benchmarking tool* supports countries in assessing the maturity of their national regulatory systems across nine core functions, including PV. Based on the results of a benchmarking exercise, identified gaps or areas for improvement in the PV system are incorporated into an institutional development plan, providing a structured, stepwise approach to strengthening regulatory capacity.

Given the shared processes and requirements in medicines and vaccine safety surveillance, the strategy encourages the dual use of data tools, methods and regulatory frameworks across both product types. It also promotes leveraging existing networks and platforms, including the WHO Programme for International Drug Monitoring, African Medicines Regulatory Harmonization, South-East Asia Regulatory Network, relevant bodies of the Association of Southeast Asian Nations, the Regional Pharmacovigilance Network of the Americas and Caribbean, the Western Pacific Regional Alliance of National Regulatory Authorities, and the Coalition of Interested Parties.

Safety communication across the product life cycle is addressed as a cross-cutting theme, with suggested methods to enhance communication. To support implementation, the strategy also includes hypothetical scenarios illustrating how its concepts can be applied to the introduction of medicines and vaccines in different settings – helping countries draft tailored PV development strategies and plans.

Success will be measured by country adoption and stakeholder engagement, with proposed indicators such as improvements in PV system maturity and other key performance metrics.


VACCINE

Introduction

Access to medicines and vaccines has increased steadily over the past two decades in low- and middle-income countries (LMICs) *(1–5)*. However, there has not been a proportionate improvement in pharmacovigilance (PV) in these settings, neither in practice nor in infrastructure. For example, more than 70% of the World Health Organization (WHO) Member States, territories and areas are LMICs.[1] They are part of the WHO Programme for International Drug Monitoring and have some PV infrastructure, yet they contribute only around 18% of the total reports in VigiBase (the WHO global database of reported adverse events of medicinal products) *(6)*. At a national level, safety data are often collected by different entities, and typically are not fully shared among various stakeholders. There is generally limited capacity to carry out routine analysis of the individual case safety reports (ICSRs) or carry out causality assessments and signal detection to inform treatment policies, guidelines or regulatory decisions. In addition, effective sharing of knowledge on known safety risks and implementation of risk minimization measures are often limited to high-income countries (HIC), resulting in avoidable harm in LMIC populations.

There is a strong case for these limitations to be considered as part of development and introduction of medicines and vaccines targeting neglected tropical and infectious diseases (e.g. Ebola, dengue, malaria, schistosomiasis, leishmaniasis, human African trypanosomiasis, chronic hepatitis, respiratory syncytial virus etc.). Many such medicines and vaccines will be used exclusively in LMICs without the benefit of any data or prior experience from HICs that, in other circumstances, provide useful guidance in terms of programmatic policies and safety monitoring in LMICs. In addition, new products for diseases that affect both HICs and LMICs may be launched simultaneously in both settings. Given their mature PV systems, HICs are likely to have sufficient PV resources to monitor and manage the safety of these new products. However, this may not be the case for LMICs. This scenario was clearly demonstrated during the coronavirus (COVID-19) pandemic. COVID-19 vaccines such as viral vector, adenovirus vector and inactivated virus were mainly introduced in LMICs. Safety data on these vaccines were limited in comparison to COVID-19 vaccines that were introduced in HICs *(7)*.

LMICs should therefore be supported with a clear strategy to build and strengthen PV systems, to effectively minimize known risks and introduce new products safely, through the identification, assessment and management of any risks associated with their use. Failure to do so risks damaging lives, wasting resources and seriously undermining public trust and confidence in the health care system, and ultimately inhibiting public uptake of new vaccines or medicines.

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[1] The World Bank defines categorizes economies according to gross national income (GNI) per capita, calculated using the 2021 World Bank Atlas method: low-income: US$ 1085 or less; lower middle-income: US$ 1086 to US$ 4255; upper middle-income economies: US$ 4256 to US$ 13 205; high-income: over US$ 13 205.

Scope of the strategy

This document advances *The global smart pharmacovigilance strategy* to build and sustain PV systems that help detect, assess, understand and prevent adverse events associated with medicines and vaccines. It combines and builds on the principles of the WHO Smart Safety Surveillance ('3S') approach *(8,9)* and the *WHO Global vaccine safety blueprint (10)*. The document describes the conceptual framework of the strategy and provides guidance on its implementation with scenarios and case studies. The concepts described address PV in the full product cycle of a medicine or vaccine. The strategy is intended for use by WHO Member States, national disease prevention, treatment and immunization programmes, regulators, PV implementation partners, donors, industry and other relevant stakeholders.


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1. Underlying principles and concepts

The global smart pharmacovigilance strategy advocates using priority medicines and vaccines relevant to country settings as a vehicle for PV system strengthening. By customizing PV strengthening activities for end-to-end safety of priority products (medicine or vaccine) in each setting, there is an immediate impact on patients/individuals that can be further developed for other products in a stepwise manner. The strategy builds on four pillars: previous efforts, lessons learnt and existing PV resources; risk-based approach and PV prioritization; work-sharing and reliance; and anchoring pharmacovigilance in the overall regulatory system-strengthening efforts.

1.1 Previous efforts, lessons learnt and existing PV resources

When the WHO Programme for International Drug Monitoring was first established in 1968 it comprised ten members, all of which were from high-income settings. To date (as of September 2025), there are 182 members. Initial efforts by WHO and its partners aimed at establishing a minimum PV infrastructure in countries, fostering a reporting culture, joining the WHO Programme for International Drug Monitoring, and using customized tools to share reports with the WHO global database, VigiBase *(6)* (see Annex 1). Countries were at different levels of capacity, and tailored approaches were made to build and enhance PV systems and functionality in respective regions. Thanks to these tailored efforts, the functionality of most PV systems advanced. It is important to learn from the approaches used to enable development of future plans and concepts that will help countries advance further, and to be able to analyse and use their data related to regulatory decisions. Lessons can be learnt from initiatives that have improved PV systems at all levels.

Global efforts

Multiple stakeholders have contributed to strengthening of PV systems at a global level. Stakeholders include global networks such as: members of the WHO Programme for International Drug Monitoring; international organizations including WHO and the United Nations Children's Fund (UNICEF), the International Council on Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), the Council For International Organizations of Medical Sciences (CIOMS), WHO collaborating centres, the Bill and Melinda Gates Foundation, Global Fund, GAVI, the Global Vaccine Data Network (GVDN); regulatory networks such as the International Conference of Drug Regulatory (ICDRA); Authorities and the International Coalition of Medicines Regulatory Authorities, professional societies such as the International Society of Pharmacovigilance (ISOP), the International Society of Pharmacoepidemiology; and the private sector represented by the International Federation of Pharmaceutical Manufacturers and Associations, and the Developing Countries Vaccine Manufacturers'

Network. Improvements in standards, case definitions, sharing and transfer of data, capacity to collect, manage and analyse data, PV methods and electronic tools, have all positively impacted the readiness of systems for safety monitoring of new medicines and vaccines or of existing products in new/vulnerable populations.

Region-specific efforts

Tailored, region-specific efforts in building PV systems have resulted in a gradual increase in the ability to detect and report safety events in countries (Fig. 1). Fig. 2 shows trends in reports shared with WHO (in VigiBase) for each region. There have been overall increasing trends in all regions both for medicines and non-COVID-19 vaccines during the period. Mass roll-out of COVID-19 vaccination resulted in the sharp spike around 2021–23 in each region.

In the African Region, efforts have focused on supporting French-speaking countries. From the early 2000s, the Centre Anti Poison et de Pharmacovigilance du Maroc (Rabat, Morocco) has provided PV training in French to several countries in Francophone Africa in addition to offering courses in Arabic to the Eastern Mediterranean Region, and had also acquired the status of a WHO Collaborating Centre for Strengthening Pharmacovigilance Practices *(11)*.

In many African countries, the concept of PV was introduced through public health programmes such as malaria and HIV *(12–14)* and subsequently extended to other pharmaceutical products.

Projects such as PAVIA *(15)* and PROFORMA that were funded by the European and Developing Countries Clinical Trials Partnership brought together academia, national regulatory authorities and public health programmes, to further strengthen PV for new medicines (e.g. regimens for multidrug-resistant tuberculosis) and the safety monitoring of mass drug administration and immunization programmes. A network of PV consultants (Pharmacovigilance Sans Frontières) established by WHO travelled across borders to consult and help build PV systems throughout Africa, enhancing the PV landscape.

Initiatives such as the African Medicines Regulatory Harmonization have provided an excellent framework to address challenges related to safety and quality of medicines and vaccines of mutual interest, through resource-sharing and regional economic platforms.

Launched as a pilot, the proof of concept of the Smart Safety Surveillance (3S) approach *(9)* has expanded into the African Union Smart Safety Surveillance (AU3S) programme, a 10-year plan to develop a centralized PV system for the region *(16)*.

A joint PV course offered by WHO in collaboration with the Uppsala Monitoring Centre (UMC) and the Health Sciences Authority, Singapore, was initiated in 2010 to reach out to countries in the South-East Asia and Western Pacific Regions. In 2015, PV inspection courses were introduced followed by joint assessments, which builds on the concept of work-sharing. The South-East Asia Regulatory Network (SEARN) *(17)* has developed approaches aligned with the objectives of *The global smart pharmacovigilance strategy,* including regional strategies to stimulate reporting and to support the integration of vigilance in the regulatory framework. In July 2024, SEARN agreed to develop a regional mechanism for monitoring priority medicines and for providing recommendations to

SEARN members on safety issues, with a particular focus on the safety of medicines during pregnancy.

The Regional Pharmacovigilance Network of the Americas promotes the exchange of information, resources and experiences between national regulatory authorities, to strengthen the vigilance of medicines and vaccine safety in the Region of the Americas *(18)*.

The above efforts reflect how strategic PV approaches have emerged from global and regional experience, with networks and stakeholders playing a key role in driving progress. Over time, these initiatives and networks have grown stronger and now serve as valuable resources for countries working to develop and strengthen their PV systems (see Annex 1).

Fig. 1. Evolution of pharmacovigilance ecosystem – regional and global efforts

African Region

2007 Introduction of annual PV Francophone course

2007 Introduction of active surveillance (malaria)

2008 Network of PV consultants for Africa

2016 Tools and training

2019 Implementation of AMRH/AVAREF

2020 AU3S formation

2021 Establishment of African Medicines Agency (AMA)

Eastern Mediterranean Region

2011 WHO Collaborating Centre for PV Practices, Morocco

2021 Establishment of African Medicines Agency

2025 Inclusion of North African countries in AMRH/ AVAREF

European Region

2010 Active surveillance of HIV medicines

2010 European pharmacovigilance directive

2012 Patient reporting

Region of the Americas

2016 WHO PV Regional Networks

South-East Asia Region

2010 PV training course for ASEAN countries started

2016 Establishment of South-East Asia Regulatory Network

Western Pacific Region

2015 PV inspection courses

2017–18 Joint assessments

Global efforts

2008 Affordable PV data management system developed for LMICs

2010 WHO-Global Fund decision to include Min PV in GF grants

2011 WHO ISoP PV curriculum developed

2018–19 Smart Safety Surveillance (3S) pilot project

Global benchmarking tool

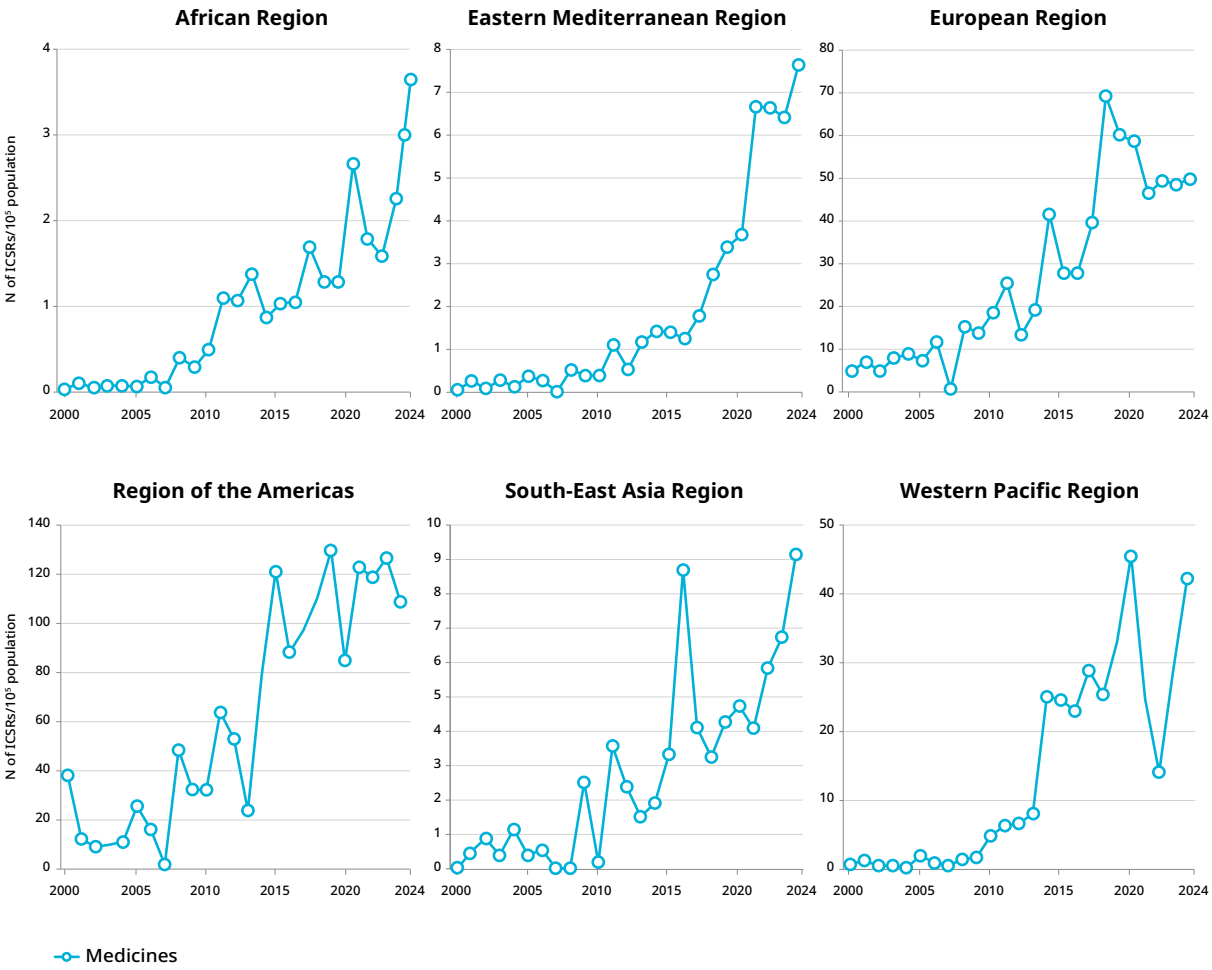
2014 WHA resolution 67.20 for focusing on regulatory systems for medicinal products

2015 Finalization of the vigilance function indicators within the WHO GBT

▼ **Annual meetings hosted in rotation by regions**

Fig. 2. Individual case safety reports submitted to WHO, by region and product type (2000–2024)

Fig. 2a. Reported ICSRs for medicines by WHO region, 2000–2024



Source: WHO global database of ICSRs (VigiBase)

Fig. 2b. Reported ICSRs for vaccines by WHO region, 2000–2024

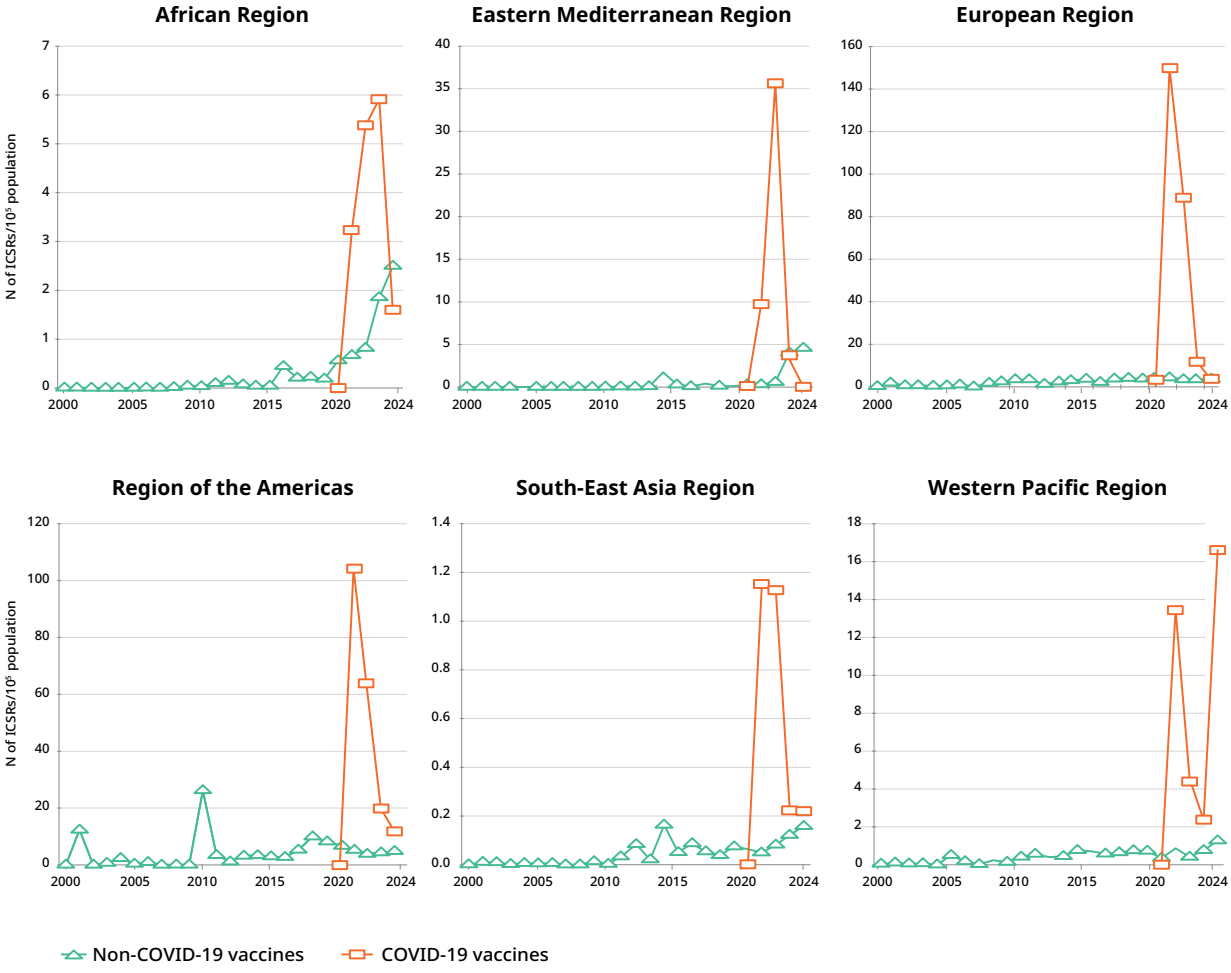
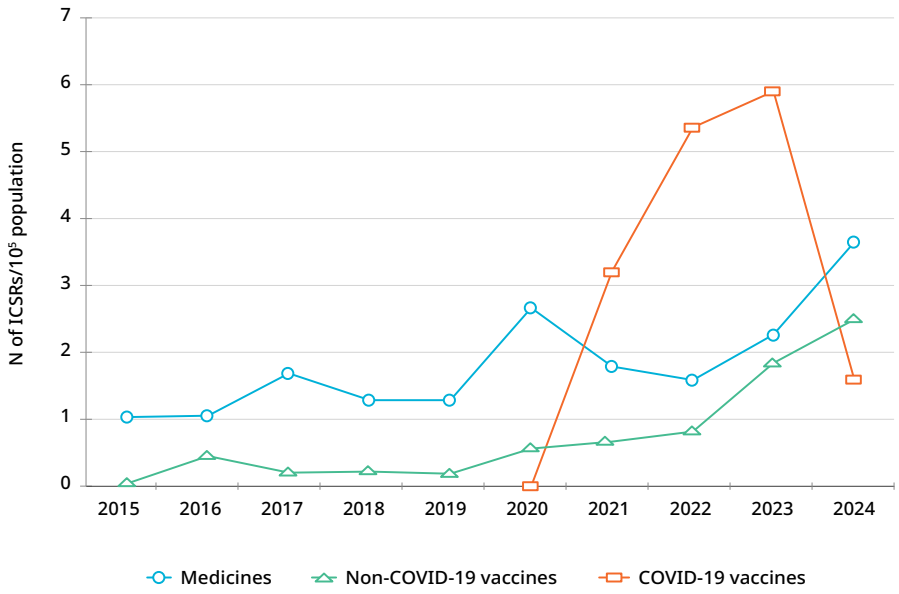


Fig. 2c. Reported ICSRs for medicines and vaccines, WHO African Region, 2015–2024



1.2 Risk-based approach and PV prioritization

Faced with competing health priorities, countries must identify where the biggest health risks lie for the population and allocate limited resources accordingly. This could be described as risk-based prioritization of resources. From a PV perspective, a given country may have hundreds to thousands of authorized medicines and vaccines, with known and unknown safety risks, usage and exposure in different population groups. Given the finite resources and the many demands facing fragile health systems, it makes sense to focus PV efforts on three types of products in LMICs:

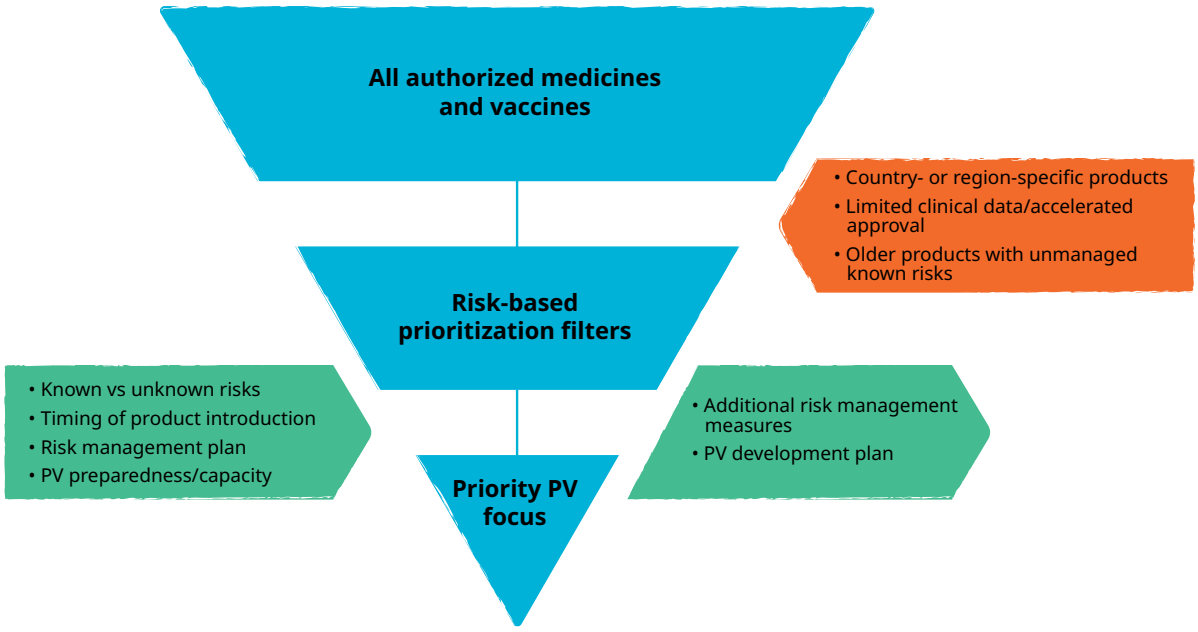
a. Products that are exclusive to a specific country or region, for example products introduced to address a disease of limited geographic prevalence (e.g. sleeping sickness), data for which will not be available or forthcoming from other countries.
b. Products with limited clinical data, receiving accelerated approval for various reasons and/or likely to be introduced worldwide, simultaneously in HICs and LMICs, with little global experience that the latter can rely on.
c. Older products with known risks that are not being managed well.

The prioritized products can act as pathfinders to building or enhancing systems that are tailored to meet the immediate PV needs, but are also resilient and sustainable for PV of additional products in the medium to long term.

When introducing a new product, or minimizing the risks of an existing product, it is important to consider the known risks (i.e. those identified in clinical trials or from real-world evidence), unknown or potential risks (sometimes described in risk-management plans), when a product will be launched, and the PV preparedness and capacity of a country or region to manage the known and unknown risks (Fig. 3).

Risk-based prioritization of pharmacovigilance activities has been applied in some countries (see Table 1). The learnings from these initiatives can guide current efforts to ensure that the PV preparedness of countries prior to the roll out of new products (e.g. the respiratory syncytial virus (RSV) vaccine and new malaria vaccines) and/or other products in the pipeline.

Fig. 3. Risk-based prioritization of pharmacovigilance activities



1.3 Work-sharing and reliance

The global smart pharmacovigilance strategy acknowledges the inequities and competing health priorities across different settings, and advocates for the prioritization of PV activities that align with available resources, through approaches such as work-sharing and reliance. Countries with less mature regulatory systems can focus on the minimum PV requirements that are needed to carry out their national PV obligations, to keep their population safe, while relying on countries with mature regulatory systems for more advanced PV activities and support. The relying authority remains independent, responsible and accountable for the decisions taken, even when it relies on the decisions, assessments and information of others. Reliance can be used in different settings for different reasons *(19)*. NRAs may favour developing and implementing effective reliance for most medicines and vaccines, and focus additional efforts only on products, issues and populations that are specific to their settings.

The 'EU-Medicines for all' procedure (EU-M4all) is an example of a reliance mechanism *(20)*. Under this procedure the European Medicines Agency (EMA) can provide scientific opinions on high-priority human medicines and vaccines that are intended for markets outside the European Union (EU). Countries outside of Europe can save precious resources, efforts and time by simply relying on the scientific opinion of the EMA, to approve the use of the product with any locally relevant adaptations to the EMA-approved risk management plan (RMP). The WHO Prequalification Programme also provides another viable model of reliance, with publicly available assessment reports that regulators and procurement agencies can rely on *(21)*.

Another way to optimize resources is through work-sharing (i.e. at a country, regional or global level). WHO defines work-sharing as a process by which NRAs from two or more jurisdictions share activities to accomplish a specific regulatory task (*19*). By establishing clear roles and responsibilities, and an agreement among stakeholders,

work-sharing prevents duplication of effort. A good example of this approach is the VigiCarib, which is a sub-regional system that Member States of the Caribbean community use to report ICSRs. This system recognizes the fact that small states have unique challenges in exercising regulatory functions such as PV due to the small populations. Opportunities for work-sharing include joint assessment of applications for authorization of clinical trials or marketing authorizations, joint PV inspections, joint post-marketing safety surveillance of medical products, and joint development of regulatory standards. Work-sharing also entails exchange of information consistent with the provisions of existing agreements and compliant with respective agency or institution legislative frameworks for sharing such information with other NRAs.

The NRAs participating in a joint assessment can combine their lists of questions or deficiencies to the manufacturer and base their respective independent regulatory decisions on the outcome of these assessments. Similarly, a joint inspection is where two or more NRAs share the activities and assessments performed during an inspection.

Table 1. Examples of applications of risk-based approaches and reliance in PV of priority products

Example of priority products (medicines and vaccines)		Impact
Medicines for diseases endemic to resource-limited settings	Bedaquiline for tuberculosis (TB)	As part of the 3S pilot, interventions to prepare countries such as Armenia, Brazil and Ethiopia for the introduction of bedaquiline showed an increase in spontaneous adverse drug reaction (ADR) reporting for TB medicines.
	Tafenoquine for malaria	Preparations made in Peru for the introduction of tafenoquine for treatment of malaria increased ADR reporting for other malaria medicines (e.g. primaquine). The introduction of tafenoquine in the Asia region provided a pathway to the concept of work-sharing through joint assessments. The work-sharing mechanism adopted for tafenoquine was sustained, and the region has later performed more joint assessments for other products.
	Fexinidazole for sleeping sickness	The EMA conducted a scientific evaluation for fexinidazole tablets through the article 58 evaluation pathway (now known as EUM4all). Countries such as the Democratic Republic of the Congo relied on the EMA evaluation, allowing the product to be accessible in the country.

Example of priority products (medicines and vaccines)		Impact
Products released in both HIC and LMIC settings with accelerated approvals or release with limited information	COVID-19 vaccines	Countries relied on assessments made by WHO PQ and emergency use listing to introduce the vaccines. And rather than develop their own systems, many countries relied on the data management systems provided by WHO, UMC and other platforms (e.g. VigiFlow, MedSafety app, District Health Information Software). As a result, there was a large volume of AEFI reports for COVID-19 vaccines in many LMICs. In the African Region, reports of AEFIs for COVID-19 vaccines received in VigiBase from 2021 now make up to nearly 40% of the total AEFI reports in the region.
	Rotavirus vaccine	Prioritized as a 3S pilot product, focused efforts on rotavirus vaccine strengthened data analyses, assessments of periodic safety update reports and RMPs, and decision-making in India.
Minimizing the risks of an older product	Miltefosine for visceral leishmaniasis and post-kala-azar dermal leishmaniasis	A safety signal of ocular disorders (including blindness) was detected through routine spontaneous reporting. Regional level work on investigating this signal included work-sharing and joint analysis of cases, and convening a multidisciplinary expert working group within the South-East Asia Region. This led to recommendations to minimize risks, including baseline eye examinations, which were subsequently adopted by the WHO Advisory Committee on Safety of Medicinal Products and applied globally.

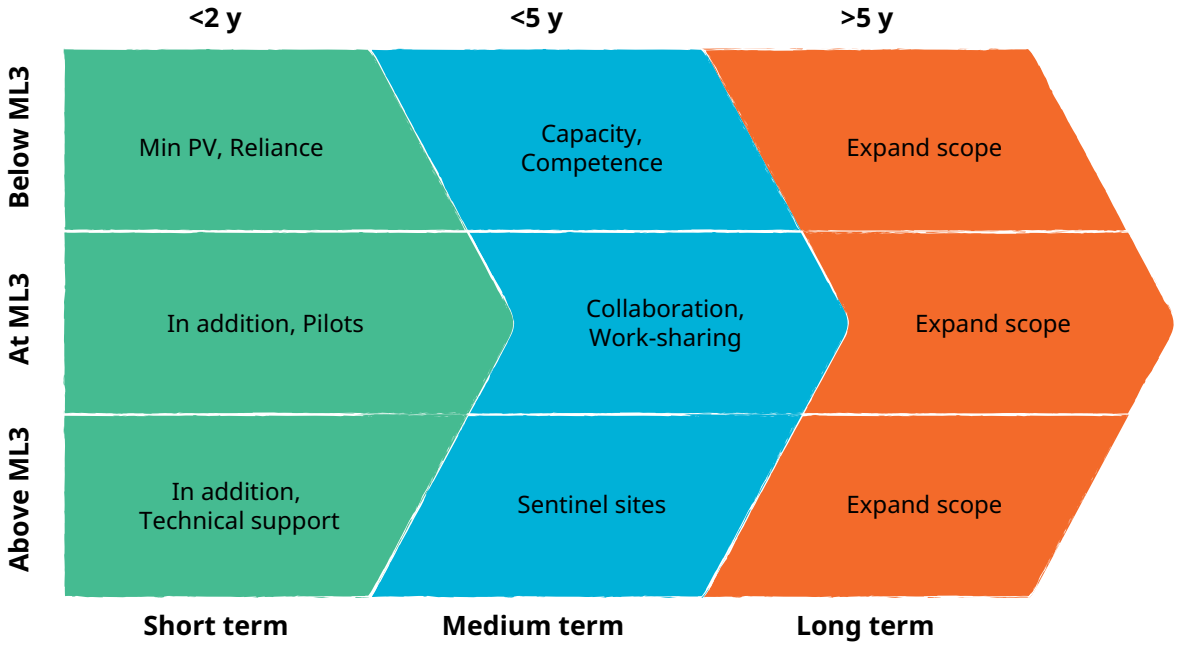
1.4 Anchoring pharmacovigilance in the overall regulatory system-strengthening efforts

Integrating PV into the regulatory system ensures regulatory ownership, and strengthens and sustains PV activities as part of the overall investment in regulatory system enhancement. In turn, PV activities support the regulator with relevant data and evidence for regulatory decisions and recommendations (see the example of Ethiopia in section 5). It is important that any effort towards building or enhancing a PV system in a country starts with a benchmarking activity, that assesses PV as a part of the overall regulatory system.

The *WHO Global benchmarking tool* assesses the maturity of a national regulatory agency (NRA). It comprises a set of indicators categorized into nine regulatory functions, including PV *(22,23)*. It is used to assign one of four maturity levels to a regulatory system. A maturity level 3 (ML3) is required in all regulatory functions for a stable, well-functioning and integrated regulatory system. Regulatory systems at ML1 and ML2 can also be considered functional if they rely on other regulators for some specific functions. ML4 is indicative of an advanced/reference regulatory system in a country. As of September 2025, twenty one countries have been assessed to have reached ML3 or ML4 in PV.

Following a benchmarking exercise, gaps and/or areas where the PV system can be improved are identified. Proposed activities to address gaps are incorporated into an institutional development plan (IDP) for regulatory system strengthening. IDPs usually consist of short-, medium- and long-term plans according to maturity level. Fig. 4 provides an overview of PV functions that can be incorporated into an IDP at varying levels of maturity. Countries that are in the early stages of building their PV systems (e.g. ML1 or ML2) might initially focus on the minimum PV requirements *(24)* while relying on countries with more advanced PV systems (i.e. ML3 or ML4) for functions such as PV inspections, assessment of RMP for products of mutual relevance, etc.

Fig. 4. System maturity levels and step-wise approach to impacting and sustaining PV systems



Note: The diagram shows increasing maturity levels from top to bottom, and short- (<2 years), medium- (less than 5 years) and long-term (five years or more) activities from left to right.

2. Implementation of *The global smart pharmacovigilance strategy*

2.1 Supporting networks

The WHO Programme for International Drug Monitoring, together with the learnings from the 3S project and the Global vaccine safety blueprint, will provide the relevant framework for the implementation of *The global smart pharmacovigilance strategy*. In addition, global and regional networks such as the International Conference of Drug Regulatory Authorities, the African Medicines Regulatory Harmonization, the South East Asia Regulatory Network (SEARN), the Pan American Network for Drug Regulatory Harmonization (PANDRH), the Global Vaccine Data Network (GVDN), will provide a platform for collaboration, expertise and resource sharing, peer learning and collective action among Member States, regions and territories. Such platforms can be leveraged to operationalize *The global smart pharmacovigilance strategy*. The UMC and other WHO collaborating centres *(25)* will also have a key role in launching and advancing the strategy.

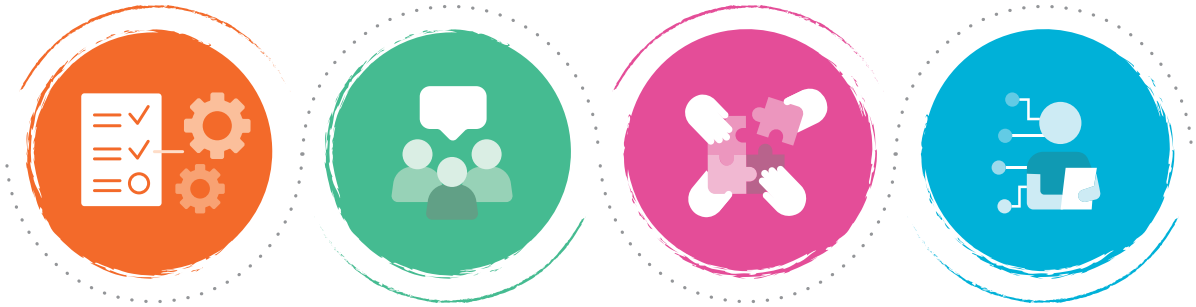
In recent times, WHO has also established a network for regulatory system strengthening, the Coalition of Interested Parties (CIP) *(26)*, which already lists PV partners such as ISOP *(27)* and the Coalition for Epidemic Preparedness Innovations (CEPI) *(28)*. Guidance on the nature and scope of collaboration between CIP partners has been developed, recognizing the increasing number of entities involved in building capacity in Member States and promoting networking, work-sharing and reliance. These will be leveraged in implementing *The global smart pharmacovigilance strategy*.

2.2 Implementation scenarios

Translating strategic principles into practical action requires consideration of the varied regulatory capacities, public health needs, and priorities of medicines available across countries. Different implementation pathways may be needed depending on whether a product is new or well-established, the maturity of national PV systems, and opportunities for regional or global collaboration. A risk-based and adaptive approach enables countries to strengthen their pharmacovigilance systems while responding to public health priorities in a feasible and sustainable manner.

Fig. 5 illustrates how *The global smart pharmacovigilance strategy* can be operationalized. In the following sections, hypothetical implementation scenarios and real-world examples are also described.

Fig. 5. Implementing *The global smart pharmacovigilance strategy*



Assessment of baseline PV system

- Assess PV system using GBT, PV indicators
- Identify gaps in PV systems
- Map gaps vs PV priorities for country, to assess PV readiness

Institutional plan

- Specific to country based on country priorities, highest risks and identified gaps in system
- Short- medium- and long-term goals

Implementation a collaboration

- Map implementation partners (WHO CCs, CIPs)
- Implement development plan
- Pursue principles of reliance, worksharing
- Participate in regional and global platforms

Monitoring

- Self-assessment (WHO KPIs)
- Re-benchmarking

Scenario 1. For countries introducing a new vaccine

Vaccine X is a new vaccine to be rolled out in multiple countries regardless of the PV maturity level (ML) in country A (ML1/ML 2 in PV) and in country B (ML3 in PV). The vaccine is aimed at preventing a fatal disease that is endemic to both countries. PV activity related to vaccine X and institutional development of the countries are conducted in parallel based on the WHO Global benchmarking tool.

In this scenario, a baseline assessment identifies key gaps in PV infrastructure and processes for country A. The short-term strategy is to address identified gaps that are essential and easily addressed. Such gaps could be lack of PV guidelines, directives, data collection and management tools. While these gaps are being addressed, country A can rely on country B (or other regional network of countries) for some of the PV functions. This reduces the workload on country A, allowing it to make a final, independent regulatory decision. In this scenario, the type of reliance described is product-specific (i.e. related to vaccine X). Work-sharing activities may be considered, including participation in a joint assessment committee for marketing authorization/ approval of vaccine X. There is also scope for reliance on product information approved by country B or reliance on the assessment of post-authorization safety study protocols and/or results. This mechanism of reliance requires assurance that vaccine X is the same or is sufficiently similar in terms of composition, indication and conditions of use in both countries.

Steps taken

Assessment of baseline PV function: Both country A and country B, are assessed for their baseline PV maturity. This can be done using the WHO Global benchmarking tool. This assesses the PV infrastructure; qualitative and quantitative aspects of PV data, including roles and systems for data management; processes such as data analysis, signal generation, use of local PV data, collaborations between PV centres and public health programmes, contribution to global database and use of global data.

Following a baseline assessment of PV function in both countries, it is found that country A does not meet ML3 requirements in PV and lacks some essential infrastructure components and processes. Country B is at ML3 in PV, however, and the approaches taken for developing the PV system in country A will be different to country B (see Tables 2 and 3).

Table 2. PV institutional development plan for country A, (ML1/ML2 in PV) planning to introduce new vaccine X

Country	Short term (<2 years)	Medium term (<5 years)	Long term (>5 years)
Country A: Minimal PV maturity (below maturity level 3 in PV)	Ensure there are: • Legal provisions, regulations and PV guidelines and SOPs for PV activities [VL01.01–06] • PV directives within the regulatory agency [VL02.01] • Integration of PV in immunization programme [VL02.02] • Reporting forms and tools (e.g. VigiMobile, VigiFlow, VigiLyze) [VL04.01] • Communication strategy [VL06.01, 02] • PV capacity for causality assessments [VL04.02] Apply principles of reliance [VL01.07] by: • Implementing passive surveillance for the new vaccine and sharing reports with relevant stakeholders and VigiBase • Using VigiBase data for national signal validation for vaccine X • Using regional data and results from studies and active surveillance with new vaccine X, for identifying unknown risks • Recognizing WHO prequalification/WHO Listed Authority (WLA)-approval of the new vaccine to adapt/ adopt the RMP for the new vaccine	• Ensure sufficient PV personnel and capacity for data analysis, and signal detection [VL03.01–04] • Set up a national AEFI review committee [VL04.06] • Participate in regional networks and platforms [VL06.03] • Ensure participation in safety communication networks such as the WHO Vaccine Safety Net (VSN) [VL06.03] • Build capacity to use WHO assessment templates to review RMPs [Vl04.04] • Pursue other activities as identified through benchmarking, as part of the implementation of the IDP to progress to ML3 in PV	Build capacity for advanced functions such as: • Establish centres of excellence for studying key PV questions • Implement safety surveillance in sub-populations (e.g. pregnant women and children) • Joint PQ and/or other regional joint assessment activities, to review RMPs • Ensure sufficient oversight for implementation of RMPs • Sustain ML3 in PV and/or work towards WLA status in PV (and/ or other regulatory functions)

Note: SOP: standard operating procedure. Relevant sub-indicators from the WHO Global benchmarking tool are shown in brackets.

Table 3. PV institutional development plan for country B (ML3 in PV), planning to introduce new vaccine X

Country	Short term (<2 years)	Medium term (<5 years)	Long term (<5 years)
Country B: Medium PV maturity (maturity level 3 in PV)	• Integration of PV in immunization programme (explore data sharing/ information technology solutions) [VL02.02 (for improvement)] • Identify adverse events of special interest (AESI) (e.g. through RMP, other sources, or existing list of AESI) prior to new vaccine roll out, and prepare for monitoring the AESI (i.e. obtain background rates) • Ensure that a risk management and communication plan are in place, to be implemented if/ when needed • Sufficient PV personnel and capacity for data analysis and signal detection • Consider complementary surveillance methods (e.g. active surveillance)	• Build capacity for active surveillance [VL04.08] • Implement safety surveillance in sub-populations (e.g. pregnant women and children) • Joint prequalification PQ and/or other regional joint assessment activities, to review RMPs • Ensure sufficient oversight for implementation of RMPs [VL04.03] • Build capacity to review periodic safety update reports [VL04.07]	• Work towards WLA in PV (and/or other regulatory functions) • Establish centres of excellence for studying key PV questions

Note: Relevant sub-indicators from the WHO Global benchmarking tool are shown in brackets.

Scenario 2. For countries introducing a new product approved by a reference authority

Medicine Y is a new medicine to be used in country C. The medicine is indicated for a neglected tropical disease endemic in the country. A baseline assessment of PV function indicates a rudimentary PV function.

Medicine Y has been reviewed under the EUM4all procedure, a procedure in which the EMA provides scientific opinions on high-priority medicines that are intended exclusively for markets outside of the EU. The evaluations are carried out in cooperation with WHO and relevant 'target' non-EU NRAs. The same rigour and standards required for marketing authorization in the EU are applied, while the benefit-risk assessment is focused on the intended non-EU population and indication(s).

Country C can use the RMP proposed by the EMA for medicine Y and adapt it for relevance, feasibility and implementation. Regulatory decision for licensing and post-authorization requirements are taken by the NRA in country C in relation to medicine Y (Table 4).

Table 4. PV institutional development plan for country C, planning to introduce new medicine Y

Country	Short term (<2 years)	Medium term (<5 years)	Long term (>5 years)
Country C: Minimal PV maturity (below maturity level 3 in PV)	Ensure there are: • Legal provisions, regulations and PV guidelines and SOPs for PV activities [VL01.01–06] • PV directive within the regulatory agency [VL02.01] • Integration of PV in corresponding disease programme [VL02.02] • Reporting forms and tools (e.g. VigiMobile, VigiFlow, VigiLyze) [VL04.01] • Communication strategy [VL06.01, 02] • PV capacity for causality assessments [VL04.02] Apply principles of reliance [VL01.07] by: • Implementing passive surveillance for the new medicine and sharing reports with relevant stakeholders and VigiBase • Using VigiBase data for national signal validation for medicine Y • Using regional data and results from studies and active surveillance with medicine Y, for identifying unknown risks • Recognizing EUM4all scientific assessments, WHO prequalification/ WLA-approval of the new medicine, to adapt/adopt the RMP for the new medicine	• Ensure sufficient PV personnel and capacity for data analysis, and signal detection [VL03.01–04] • Set up a national committee for safety of medicines [VL04.06] • Build capacity for active surveillance [VL04.08] • Participate in regional networks and platforms [VL06.03] • Build capacity to use WHO assessment templates to review RMPs [VL04.04] • Build capacity to review periodic safety update reports [VL04.07] • Pursue other activities as identified through benchmarking, as part of the implementation of the IDP, to progress to ML3 in PV	Build capacity for advanced functions such as: • Establish centres of excellence for studying key PV questions • Implement safety surveillance in sub-populations (e.g. pregnant women and children) • Joint PQ and/or other regional joint assessment activities, to review RMPs • Ensure sufficient oversight for implementation of RMPs • Sustain ML3 in PV and/or work towards WLA in PV and/or other regulatory functions

Note: SOP: standard operating procedure. Relevant sub-indicators from the WHO Global benchmarking tool are shown in brackets.

Scenario 3. Risk-based approach to address a known adverse event with an existing product

Product Z has been in use in country D and worldwide for several decades, and is associated with a well-known teratogenic effect causing developmental delays and malformations. Product Z is used for a serious disease and is highly effective. With time, as alternative treatments with similar effectiveness have become available, recommendations for use of product Z in women and girls of childbearing potential have changed.

Risk management plans (RMP) exist to manage the known risks associated with the product. But despite this, there are still many children born with malformations and developmental disorders in country D , and in other countries, due to the use of this medicine during pregnancy.

Country D and other countries in the region have heterogeneous regulatory capacities but are generally between level ML2 and ML3 in PV. As part of the regional network, the countries can review the existing RMP and measure its effectiveness (e.g. through drug utilization studies, awareness surveys among health professionals or patients, and/or by monitoring reports of malformations/developmental delays with the use of this medicine).

Depending on the findings, additional risk minimization measures could be developed regionally and introduced nationally. This could include pregnancy prevention programmes, awareness campaigns, education of health care providers and patients, information materials in local languages etc. Work-sharing at a regional level could be adopted to pool resources into the development of these measures. The regional network could also design and implement studies to understand the effectiveness and impact of these additional measures (Table 5).

Table 5. PV institutional development plan for country D, planning to continue using product Z

Country	Short term (<2 years)	Medium term (<5 years)	Long term (>5 years)
Country D	Introduce risk minimization measures: • e.g. package labelling, patient information leaflets, patient education materials, pregnancy prevention programmes, annual reviews [VL04.04] Introduce communication strategies to communicate measures: • e.g. campaigns, dear Dr letters, educational materials [VL06.02] Collaboration with national public health programmes [VL02.02]	Monitor the usage of product Z [VL04.05] Survey to understanding knowledge and practices of doctors and patients [VL04.08]	Monitor impact of risk minimization measures (e.g. reduction in number of adverse drug reactions) [VL05.02]

2.3 Implementation of the key concepts of the global smart pharmacovigilance principles in safety monitoring of COVID-19 vaccines

On 30 January 2020, WHO declared the COVID-19 outbreak a public health emergency of international concern. Numerous vaccines, developed using novel platforms and technologies, were swiftly approved to contain the pandemic, but there was limited information on the use of these vaccines in large populations and on their long-term or rare adverse events. It was therefore crucial to ensure that infrastructure and capacity for monitoring the safety of COVID-19 vaccines were in place worldwide, with existing infrastructures reactivated and engaged before the introduction of vaccines.

WHO primarily focused its efforts on supporting LMICs in the application of the smart pharmacovigilance principles, to monitor the safety of these vaccines, although elements of these principles were apparent universally, across both HICs and LMICs.

Leveraging previous efforts and existing resources

In preparation for the deployment of vaccines, national and global efforts were made to plan activities using learnings from previous experiences. For example, the European Region used the experience gained during the 2009 H1N1 influenza pandemic to form a pharmacovigilance plan for the EU regulatory network for COVID-19 vaccines *(29)*. The Global Vaccine Safety Blueprint *(10)* formed the basis of the COVID-19 vaccine safety surveillance strategy. Tools and methods developed as part of the blueprint were adapted and used. Together with the WHO experiences from H1N1 and Ebola epidemic informed the WHO COVID-19 vaccines safety surveillance manual that guided countries in preparing for the introduction of COVID-19 vaccines *(30)*. Checklists were developed to determine country preparedness for vaccine introduction.

Existing tools, such as the Safety Platform for Emergency Vaccines (SPEAC) definitions and a list of adverse event of special interest (AESIs) were adapted to cover potential and known safety issues for COVID-19 vaccines. Such definitions made it easier to describe and define adverse event following immunization (AEFIs) such as myocarditis/pericarditis.

Established networks such as the WHO Programme for International Drug Monitoring and the Global Vaccine Drug Network used their systems to share data, detect and investigate signals *(31,32)* and AESIs *(10)*. The WHO Collaborating Centre for International Drug Monitoring (Uppsala Monitoring Centre), that manages VigiBase *(6)*, performed descriptive analysis and signal detection on accumulating data with the new COVID 19 vaccines.

Tools such as WHO AEFI reporting forms, active surveillance protocols, and the anaphylaxis management guide, were adopted to be more applicable to COVID-19 vaccine safety *(33–36)*.

Strengthening pharmacovigilance as part of regulatory system strengthening

Gaps in PV infrastructure, stakeholder engagement/collaboration, and the capacity to process and analyse data can be identified through assessment tools such as the WHO Global benchmarking tool. This tool was used and adapted by several countries in preparing for the launch and safety monitoring of COVID-19 vaccines (Box 1). Regional authorities such as the EMA stepped up their efforts as well in responding to PV needs during the pandemic.

Box 1. Examples of WHO Global benchmarking tool adoption during COVID-19 pandemic

Pakistan. PV efforts were based on findings from a benchmarking assessment in 2019. Activities included revision and development of regulatory policies and guidelines for AEFI surveillance. A national action plan for safety surveillance of COVID-19 vaccines was formed, connecting different stakeholders and facilitating coordination. Existing AEFI committees were revitalized, and a PV risk assessment expert committee was established. Information technology solutions to facilitate seamless transfer of electronic data were implemented, and extensive capacity building was organized *(37)*.

South Africa. Before the COVID-19 vaccine roll out, the regulatory system met WHO minimal capacity standards for vaccine safety (i.e. collating and managing AEFI data, monitoring and investigating AEFIs, and completing causality assessments). Identified gaps included low reporting and lack of tools for data linkage between the national AEFI database – held by the national immunization programme – and the national PV centre, the South African Health Products Regulatory Authority. A digital reporting application (medSafety) was introduced, with a campaign to increase awareness of AEFI reporting systems among health care professionals and facilitating public reporting *(38)*.

European Medicines Agency. Existing procedures for signals to be presented at the Pharmacovigilance Risk Assessment Committee were made more agile to accommodate the large volume of safety data collected and the urgent demand for rapid signal detection. In some instances, the signal procedure and time between meetings were shortened from the usual 60 days to two weeks. Existing public communication tools were enhanced to increase transparency. International collaborations between regulatory and public health agencies were established through the International Coalition of Medicine Regulatory Authorities, and supported the exchange of information, strategic directions, and work-sharing among regulators and research institutions to address common challenges *(29)*.

Work-sharing and collaboration

The COVID-19 pandemic required a global approach to rapidly detecting and managing risks resulting from AEFIs. This was crucial to prevent harm, increase public confidence in the vaccination programme, reduce hesitancy, and protect the public from severe disease, hospitalizations and deaths. Work-sharing and collaboration occurred between countries in given regions, as well as globally.

European Medicines Agency regional networks provided a model of how PV could be coordinated. Data and expertise were shared among countries through meetings of the Pharmacovigilance Risk Assessment Committee. This regional mechanism promptly discovered a rare and serious AEFI, namely thrombosis with thrombocytopenia syndrome *(36)*.

Initiatives such as the African Union Smart Safety Surveillance (AU-3S), invested in activities to strengthen PV at the regional level. Countries participating in AU-3S benefited from sharing experiences and best practices. Technical expertise was enhanced by establishing a multi-country experts' group to assess signals. This signal management group is expected to serve as the foundation of a joint signal management and a Pharmacovigilance Risk Assessment Committee in the African Union.

Each week during the pandemic, WHO and its Collaborating Centre for International Drug Monitoring (UMC) shared a descriptive analysis of spontaneous reports on COVID-19 vaccines from the global database, VigiBase *(39)*. This service was particularly important since data on vaccines used outside the EU and the United States of America were limited, and countries could rely on the global data from VigiBase. VigiBase safety data on COVID-19 vaccines facilitated the detection of AEFI signals (e.g. tinnitus), underscoring the importance of sharing data and strengthening the evidence for signals *(40)*. The WHO Global Advisory Committee on Vaccine Safety utilized VigiBase data and other sources to advise on any observed and emerging risks with the vaccines *(41)*.

The vaccine AEFI data, which had previously been quite limited, increased significantly during the pandemic. While tremendous public awareness certainly contributed to this increase, reporting was improved in general, and is being sustained in many countries. This observation underscores the founding principle of *The global smart pharmacovigilance strategy:* that by focusing selectively, but comprehensively, on the most urgent issues, it is possible to build a lasting infrastructure and practice.

Overall success

Even though the COVID-19 pandemic was unprecedented in its scale and scope, it also presented an opportunity to advance vaccines PV on a global scale. Global vaccine AEFI data, which had been quite limited in VigiBase, increased significantly during the pandemic. No doubt the tremendous public awareness contributed to this increase, but overall reporting has also improved and is being sustained in many countries. This observation underscores the founding principle of *The global smart pharmacovigilance strategy,* that by focusing selectively and comprehensively on the most urgent issues, it is possible to build a lasting PV infrastructure and practice.

These collaborative efforts not only enhanced vaccine safety during the COVID-19 pandemic but also laid the groundwork for more resilient PV systems – reinforcing the strategic importance of integrating PV into broader emergency preparedness frameworks, as outlined in Annex 2.

2.4 Introduction of bedaquiline and delamanid for multidrug-resistant tuberculosis

Multidrug-resistant tuberculosis (MDR-TB) is caused by *Mycobacterium tuberculosis* that is resistant to isoniazid and rifampicin, the two most effective first-line tuberculosis (TB) drugs *(42)*. In 2023, over 400 000 of the 10.8 million TB cases were MDR- or rifampicin-resistant *(43)*. MDR-TB is harder to treat than drug-sensitive TB, with longer regimens, more side-effects, lower survival rates, and higher associated costs. Many untreated patients die or become chronic carriers, spreading the disease *(44)*.

In 2014, the World Health Assembly approved a strategy to reduce TB deaths by 95% and incidence by 90% between 2015 and 2035. The new drugs bedaquiline and delamanid were introduced, and together with the use of regimens containing linezolid and clofazimine the TB treatment landscape was modified *(45)*. Initially, there was a conditional regulatory approval of the two new medicines by the European Medicines Agency and, in the case of bedaquiline, by the United States Food and Drug Administration (US FDA) *(46–48)*. The introduction of bedaquiline and delamanid is an example of access of a new product authorized for use across HICs and LMICs. PV systems operating in collaboration with TB treatment programmes were promoted and supported to provide ongoing safety monitoring. Various initiatives contributed to this, including the WHO Smart Safety Surveillance pilot project (focused on bedaquiline), the Expand New Drug Markets for TB consortium, and Challenge TB led by KNCV Tuberculosis Foundation. Support was provided to several countries including Armenia, Brazil, Ethiopia, Indonesia, Kyrgyzstan, Peru and Ukraine.

Risk-based prioritization

The conditional approval of bedaquiline was based on incomplete safety data, with concerns about cardiac QT-interval prolongation, other cardiac events, increases in hepatic transaminases and associated deaths. The US FDA issued a warning about increased mortality and QT prolongation with bedaquiline. Further studies were required to assess the risks of combining bedaquiline with other medicines. Strengthening PV was essential for monitoring the safety of these new TB treatments.

Bedaquiline and delamanid, as well as established products used in new regimens (e.g. linezolid and clofazimine), were prioritized for safety monitoring. Due to existing concerns about prolonged QT intervals and cardiac events, countries focused on these signals and related potential risks.

In Armenia, Brazil, Ethiopia, Peru and Ukraine, a baseline assessment of PV systems was conducted using a set of indicators derived from the WHO Global benchmarking tool. Based on the assessment, a tailored approach was taken in each country, to focus on the identified gaps and strengthening the PV systems sustainably, to obtain

safety data on priority products that could be shared and pooled globally *(22)*. For example, Armenia focused on collaboration and data sharing between TB and PV programmes, increasing the frequency and quality of reporting by introducing technical solutions (such as a reporting app), and strengthening structures like expert advisory committees. Meanwhile, Brazil, Ethiopia, Indonesia and Peru implemented active surveillance methods and causality assessments. Kyrgyzstan introduced PV tools such as VigiFlow, and standardized reporting forms, as well as building PV awareness in collaboration with the TB programme. In Ukraine the focus was on signal detection, formation of expert advisory committees, and strengthening collaboration with the TB programme.

Work-sharing was demonstrated within countries through multi-stakeholder collaborations, and globally through pooling of data (from both spontaneous reporting and active surveillance of adverse events). Stakeholders included the Expand New Drug markets for TB consortium (comprising Médecins Sans Frontières, Partners in Health, and Interactive Research and Development, and the KNCV Tuberculosis Foundation), industry (Janssen, which donated the medicine), national TB and PV programmes, and WHO. This was an opportunity for different stakeholders to work synergistically and efficiently by taking up different roles. For example, in Armenia, Médecins Sans Frontières carried out the active surveillance of bedaquiline, while WHO and the national TB and PV programmes supported the transfer of safety data collected by MSF to the PV centre, which then shared it with VigiBase. Globally, WHO supported the pooling of data by providing tools and training to facilitate data transfer of ICSRs to VigiBase that was then routinely analysed by UMC and reviewed by the WHO Advisory Committee on Safety of Medicinal Products. In addition, WHO established an active TB drug safety monitoring and management system to pool data from active surveillance methods. The countries with limited resources for scientific evaluation or signal detection could rely on the scientific assessment by UMC and the recommendations from the WHO advisory committee, the EMA and the US FDA, while retaining the autonomy to adapt the recommendations to their settings.

Following the early introduction of bedaquiline and delamanid, the prioritized and coordinated efforts to monitor their safety have led to a greater understanding of their safety profiles, supporting their safe use, and revolutionizing current TB treatment opportunities. In addition, these efforts have improved collaboration between TB programmes and NRAs, integrating smart PV principles within both.

3. Enhanced safety communication

Safety communication and social engagement – especially for preventive medicines and vaccines – are essential cross-cutting elements of *The global smart pharmacovigilance strategy.* Addressing safety concerns protects patients and increases confidence in public health programmes, particularly immunization programmes that may face challenges associated with vaccine hesitancy. It is also important to promote understanding through the media and health literacy among the public so that they can discern between well-founded medical information and misinformation. Communication on the safety of medicines and vaccines is necessary throughout the life cycle of a product, and not just as part of a crisis management plan.

Communication can be enhanced by:

- Strengthening the capacity and infrastructure of PV systems to communicate product safety information and manage the communication response to vaccine and medicine safety-related events.
- Identifying and characterizing product safety concerns among the public, health care workers, and other stakeholders as potential safety signals that warrant further investigation and a communication response (e.g. through communication campaigns such as MedSafety Week).
- Providing timely, short and clear messages to all stakeholders during a crisis, describing what is known, what is not known, and what is being done to fill these gaps.
- Building/strengthening infrastructure (e.g. by identifying expertise and formulating a communication strategy).
- Training health care workers and decision-makers on vaccine and medicines safety, and introducing continuing education programmes that include interpersonal and risk communication skills development.
- Engaging the media and civil society regularly about PV, particularly prior to introducing new medicines and vaccines, or when a related issue arises
- Supporting the development of trustworthy websites and social media channels for vaccine safety information and linking with the WHO Vaccine Safety Net *(50)*.
- Investing in the development of innovative tools for engaging with stakeholders and support initiatives, and interventions for effective management and dissemination of safety information in the digital space.

The WHO Vaccine Safety Net (VSN) is a global network of websites established to provide reliable information on vaccine safety *(49)*. As of the end of August 2025, 117 websites from 50 countries are part of VSN, offering information in 41 languages. VSN serves as an important resource for authorities seeking reliable, science-based information on vaccine safety, and can be leveraged in strengthening safety as part of *The Global smart pharmacovigilance strategy.*

4. Measuring the uptake and impact of *The global smart pharmacovigilance strategy*

It is important to monitor the implementation of *The global smart pharmacovigilance strategy* and its impact. The uptake of the strategy can be measured as the number of adopting countries and stakeholders contributing to its implementation. Such data could be collected through a survey among Member States and feedback from the Coalition of Interested Parties (CIP). Several uptake and impact metrics are proposed:

- Number of countries/regions with a list of priority products that form the focus of PV developmental activities in the country, with a clear rationale for their inclusion in the list, and related PV activities.
- Number of countries/regions with a risk-register of known adverse events/AESIs, and activities that are designed to measure/study/review these AESIs.
- Number of countries participating in regional platforms activities (i.e. as an indicator of reliance, and work-sharing).
- Number of countries/regions using VigiBase data for signal validation (i.e. as an indicator of reliance on VigiBase).

Qualitative and quantitative measures will be used to study the impact of the strategy. This includes reports in VigiBase, quality of reports, changes in PV system maturity compared to baseline assessment, uptake of safety communications, periodic safety update reports and RMP assessments.

Additional measurable indicators can be used to evaluate the impact of the strategy in terms of system strengthening and safety information on a product (i.e. medicine or vaccine) through its life cycle, adoption of the principles of reliance and work-sharing, integration of PV into public health systems, and improvements in key performance indicators (e.g. the number of countries reporting at least one serious AEFI reported per 1 million total population per year). The impact on a product can be measured by understanding if risks have been identified through the characterization of the safety profiles, detection of signals and decisions made (see Table 6).

Baseline and follow-up assessment of current maturity level in PV will be carried out, globally and at the regional level, as relevant tools (interviews, surveys) used to measure the impact of previous approaches (GVSB, 3S) will be reviewed, expanded, and adopted to capture information on the awareness and uptake of the strategy, national commitments, investments and use of risk minimization measures etc.

Table 6. Proposed indicators of uptake and impact of *The global smart pharmacovigilance strategy,* as of 5-years post-launch and measured against baseline data

Impact area	Indicators/metrics	Method/source of data
Country engagement	Number of countries adopting strategy	Survey of Member States and/or other communications to WHO
Stakeholder engagement	Number of stakeholders contributing to implementation of strategy	Coalition of Interested Parties records and stakeholder survey
Risk-based approach	Prioritization of PV activities	Institutional development plans identified in WHO records Priority list of products to be monitored (from country or regional networks records) Priority list of AESIs (country or regional network records)
Mutual reliance work-sharing and collaboration between Member States on PV	Participation in WHO Programme for International Drug Monitoring Contribution to VigiBase Joint assessments Data on collaborative agreements between countries	WHO Programme for International Drug Monitoring membership records VigiBase reporting statistics/ dashboards Data from regional networks Survey and/or WHO data (e.g. regulatory convergence and networks)
Strengthened PV systems	Number of countries with an improvement in WHO Global benchmarking tool maturity level for PV compared with ML at baseline	WHO regulatory benchmarking records

Impact area	Indicators/metrics	Method/source of data
Improved functionality of PV systems	Number of countries reporting at least one serious AEFI per 1 million population per year	WHO records
	Total number of adverse drug reaction reports received in the past three years (also expressed as number of adverse drug reactions per 100 000 population).	Regulatory websites, regional platforms
	Characterization of safety profile and signal detection (i.e. meeting with safety advisory groups)	Alerts to WHO, regulators websites, Vaccine Safety Net
	Decisions made based on data obtained (i.e. regulatory updates)	Landscape analyses (with baseline data available)
	Communication of findings/ identified risks	
	Number of countries implementing active surveillance	
	Number of countries with safety monitoring in sub-populations	

5. Applying the principles of *The global smart pharmacovigilance strategy*: case studies from countries

Brazil. From signal to regulatory action: smart, focused and lasting actions

In 2023, the Region of the Americas experienced a surge of 4 million dengue haemorrhagic fever cases across 46 countries, a threefold increase compared to previous years. Brazil accounted for approximately 70% of these reports.[2] In response to this escalation, the Brazilian Health Regulatory Agency (Anvisa) evaluated the safety, efficacy and quality of the tetravalent live attenuated dengue vaccine (Qdenga®) and approved its use in the country for individuals aged 4 to 60 years. Following this approval, the manufacturer sought the inclusion of this vaccine in the Unified Health System (SUS), which was granted by the National Commission for Health Technologies Incorporation in SUS (Conitec) in December 2023. Consequently, Brazil became the first country to introduce Qdenga® into its National Immunization Programme (PNI).

WHO and the Pan American Health Organization (PAHO) reviewed the available evidence and published guidelines to support dengue vaccination, recommending Phase 4 studies to monitor vaccine safety and efficacy. Considering the limited vaccine supply – 6.5 million doses in the first year, with 1.5 million allocated for the initial phase – and the recommendations from PAHO/WHO and the Technical Advisory Committee on Immunization, Brazil launched its dengue vaccination strategy on 9 February 2024.

The campaign commenced with the distribution of 1.5 million doses to 521 municipalities in high-transmission areas, prioritizing children and adolescents aged 10 to 14 years. To ensure robust safety monitoring, the Ministry of Health implemented a PV plan to strengthen the monitoring of AEFIs. Within a month, the pharmacovigilance PV team identified an unexpected increase in hypersensitivity reactions, including anaphylaxis (43.8 cases per 100 000 doses administered) and anaphylactic shock, with rates up to four times higher than expected.[2] In response, the Ministry of Health activated the Interinstitutional Committee on Vaccine Pharmacovigilance and Other Immunobiologicals and the Technical Advisory

[2] Data are sourced from national authorities and may not represent WHO official statistics. These figures should be interpreted within the context of the reporting country's health systems and surveillance capabilities.

Committee on Immunization, bringing together experts from Anvisa, the National Institute for Quality Control in Health (of the Oswaldo Cruz Foundation), PAHO/WHO, and scientific societies. This collaborative effort resulted in a technical note being published providing guidelines to ensure the safe administration and safety surveillance of the dengue vaccine.

A crisis communication strategy was implemented, starting with a press conference led by the Minister of Health and representatives from key institutions, including Anvisa and PAHO/WHO. Clinical trials on Qdenga® had not previously identified anaphylaxis as a post-vaccination event. However, given this safety signal and similar notifications in other countries, Anvisa requested the marketing authorization holder to include anaphylaxis as a possible adverse event in the Qdenga® vaccine package insert, and updating of the vaccine's RMP.

PAHO coordinated regional discussions and promoted international cooperation to enhance vaccine safety surveillance and improve safety monitoring. Meetings with global experts were held (with the Global Advisory Committee on Vaccine Safety and the WHO Programme on Vaccine Safety), and a webinar was organized, where Brazil and Argentina shared their experiences with introducing the vaccine. Brazil also implemented additional measures, such as a risk-benefit assessment of vaccination, a case-control study was initiated to investigate associated risk factors, and partnership with research institutions to analyse potential allergens and mechanisms involved in post-vaccination anaphylaxis. Anvisa continues monitoring the vaccine through the assessment of the Periodic Benefit-Risk Update Report and other coordinated measures with the Ministry of Health.

PAHO/WHO developed monitoring guidelines, including a diagnostic algorithm for dengue in vaccinated individuals, trained stakeholders on anaphylaxis detection and management, and developed protocols for monitoring inadvertently vaccinated pregnant women. Currently, Argentina, Brazil and Peru have incorporated the Qdenga® vaccine into their national dengue prevention and control strategies. The mechanisms of anaphylaxis and vaccine-associated enhanced disease continue to be investigated, while regional initiatives focus on integrating dengue surveillance systems with vaccine safety monitoring.

Egypt. Enhancing AEFI data management through collaboration and adaptation of existing infrastructure

In Egypt, the Ministry of Health and Population has been instrumental in advancing the country's PV and vaccine safety monitoring efforts, through a collaborative approach involving the Egyptian Pharmaceutical Vigilance Center, the Egyptian Drug Authority and the Expanded Programme for Immunization. The responsibility for surveillance of AEFIs is shared between these key stakeholders, each playing a crucial role in ensuring the safety of vaccines administered across the country.

The Expanded Programme for Immunization closely monitors vaccines distributed through campaigns and routine immunization programmes, ensuring that all AEFIs are reported and serious cases are promptly investigated. The Egyptian Pharmaceutical Vigilance Center processes AEFI reports and identifies safety signals and alerts the stakeholders of anything unusual. The collaboration ensures proper collection,

assessment and interpretation of AEFI data collected from all sources, including spontaneous reports from health care professionals, the public, and marketing authorization holders for timely decision-making.

A decision was made to digitalize the system to enable the country to integrate AEFI reporting and management into existing health systems, allowing real-time AEFI surveillance with rapid safety signal detection and improved efficiency. It was also hoped that raising awareness among communities about the importance of AEFI reporting and the benefits of immunization would promote vaccine confidence and uptake.

Previously, AEFI reports in Egypt were mainly collected manually (i.e. paper-based reporting) in vaccination centres, hindering non-serious cases reaching the central level of the Expanded Programme for Immunization and Egyptian Pharmaceutical Vigilance Center in real-time. The introduction of electronic reporting platforms marked a significant improvement in how these reports are collected and processed.

VigiFlow, the data management system offered by WHO/UMC to Member States has been in use in Egypt since 2013 for reporting and managing medicines-related adverse events. The decision to adopt a single VigiFlow interface for both vaccines and medicines – or maintaining two separate interfaces – required careful consideration, especially because of the differing monitoring and reporting requirements. Following discussions with all stakeholders, the dual interfaces approach (i.e. separate for medicines and vaccines) was adopted. However, building on previous experience, existing technical know-how, support, training, feedback and monitoring was used to support AEFIs reporting.

The country plans to provide additional training and capacity-building programmes for health care professionals, surveillance officers, and national officials in both the Egyptian Drug Authority and the Expanded Programme for Immunization. Strengthening data quality and analysis is planned to better understand AEFI trends, identify areas for improvement, and inform immunization policy decisions.

Ethiopia. Prioritization for improved signal detection

To address the need for improved related signal assessment, Ethiopia prioritized PV activities of two new products for treating high-burden diseases: bedaquiline for MDR-TB and tafenoquine for malaria (caused by *Plasmodium vivax*). Sensitization of health care professionals through a campaign around the introduction of a safety reporting app, training programmes for advisory committee members, and other activities that focused on these products improved collaboration with public health programmes, raised awareness of ADR reporting, and enhanced the integration of PV into public health programmes. Technical support was provided by various stakeholders, including the PAVIA and PROFORMA projects, UMC, the United Kingdom Medicines & Healthcare Products Regulatory Agency (3S pilot), and WHO, among others. This support included active surveillance for anti-TB medicines, human capacity building, twinning with other regulatory agencies, organizing workshops and improving regulatory frameworks,

The PV journey to ML3 was a stepwise process, starting with a baseline assessment, developing a roadmap and creating a PV country strategy. Collaboration with various stakeholders was crucial in building capacity. Assessment with the WHO Global benchmarking tool identified gaps in communication of medicine safety information, lack of standard operating procedures, and insufficient human resources. An IDP was elaborated to include restructuring the PV unit, increasing staffing, developing legal and quality management system documents, improving communications, and decentralizing PV activities to university hospitals.

PV efforts are being sustained through close follow-up, including regular meetings with stakeholders and supportive supervision of health facility reporting. Clear terms of reference for the PV Advisory Committee ensures adherence to agreed procedures, regular meetings and clarity of functions, and the government allocates a budget for PV activities.

Indonesia. Focusing on a priority product to integrate pharmacovigilance into TB treatment programmes

Tuberculosis (TB) has long been a public health concern in Indonesia, which has the second highest prevalence of TB globally. Addressing these challenges requires strong commitment and leadership from national and sub-national stakeholders. The Indonesian Food and Drug Administration (BPOM) is mandated to ensure the safety, efficacy and quality of pharmaceutical products, including supporting public health programmes through regulatory functions such as PV.

Efforts to improve PV for medicines used in public health programmes such as HIV, TB and malaria included developing a specific PV guideline in 2016 with the support of Global Fund. However, the implementation of the guideline was sub-optimal and largely ineffective. Indonesia struggled with under-reporting of adverse events (AEs). One of the main contributing factors was the heavy workload of health care professionals, who prioritized clinical management of adverse events once detected. Reporting was done manually on hard-copy forms (and sent to BPOM by post or email).

The situation was addressed through systematic changes at all levels. With support from WHO in 2016–2017, the Indonesia TB programme piloted use of the new anti-TB medicine, bedaquiline. In collaboration with the Ministry of Health, BPOM conducted a cohort event monitoring study, focusing on the risk of QT prolongation. The study provided experience in active safety surveillance. Health care professionals were sensitized to drug safety monitoring and the number of reports of AEs increased. However, the TB programme and BPOM were operating on two different reporting systems, which led to considerable duplication of efforts.

MoH and BPOM collaborated to find an information technology solution so that health care professionals could report AEs once, through a common portal. Mapping of core variables between the two reporting systems was conducted and an automated bridge synchronized reporting and shared reports to BPOM from both systems. Following a pilot phase the new system was launched and AE reporting for TB medicines increased significantly. As a result, the analysis of PV data has enhanced the PV centre capacity through feedback of potential signals, collaboration with other stakeholders has strengthened, guidelines have been revised and data quality has improved.

To ensure continuous improvement of TB medicines safety monitoring, BPOM and the Ministry of Health developed an IDP with resources allocated for regular monitoring and evaluation meetings, AE report evaluations with PV experts, periodic staff training, and system updates to enhance integration.

Indonesia's efforts align with *The global smart pharmacovigilance strategy,* and feature intersectoral collaboration through the IDP. Strong leadership and commitment at all levels were supported by a clear regulatory framework, information technology support, and budget allocations. Key performance indicators were set annually, with regular monitoring, evaluation and staff training for continuous improvement.

In Indonesia, safety monitoring of TB medicines was prioritized due to a previous lack of accountability. The focused efforts created a successful model for integrating PV into public health programmes and demonstrated the effectiveness of *The global smart pharmacovigilance strategy.*

Japan. Fostering work-sharing and reliance in pharmacovigilance

The Pharmaceuticals and Medical Devices Agency (PMDA) of Japan is the regulatory authority for medical products, including medicines and vaccines. The PMDA plays an important role in the field of PV in the country, regionally and globally, collaborating with domestic and international stakeholders, including overseas regulatory authorities and WHO, to collect and evaluate safety information, to implement measures to protect patient safety, and to set international standards.

As one of the founding regulatory members of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), PMDA has actively participated in the development of ICH guidelines related to PV and has fully implemented them in the national regulatory system. Notably, the E2 series of ICH guidelines provides processes and standards for the collection, reporting and evaluation of safety information. Additionally, the Medical Dictionary for Regulatory Activities (MedDRA) is the multilingual dictionary used to standardize the reporting of AEs. PMDA utilizes the ICH guidelines and MedDRA to enhance the consistency and accuracy of globally collected medicines safety information, which serves as the basis for effective international cooperation.

In Japan, efforts are being made to advance reliance, which involves utilizing the data and evaluation results of other countries' regulatory authorities in pharmacovigilance *(50,51)*. These data and results are obtained from both published documents and information from the regulatory networks.

PMDA is also promoting the concept of reliance among Asia Pacific countries, where PMDA collaborates with regulatory authorities to share information and provide technical support related to PV. For example, through the Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs, PMDA offers regional training programmes for regulatory officials to enhance their knowledge and skills in pharmacovigilance.

These initiatives have led to the rapid and efficient collection and evaluation of safety information, thereby improving patient safety. Furthermore, cooperation with regulatory authorities in other countries has strengthened the PV systems in the region. However, the reliance approach presents some challenges as it requires reliability in the data and evaluation results of other countries' regulatory authorities, which can be sometimes difficult to ensure. Effective cooperation with other national regulatory authorities necessitates understanding institutional and technical differences, and smooth communication is essential to overcome these challenges.

Moving forward, PMDA plans to undertake the following initiatives to strengthen and streamline PV systems:

- Expand the use of real-world evidence and consider introducing advanced information collection and evaluation systems utilizing technologies such as those aided by artificial intelligence.
- Deepen existing collaborations with regulatory authorities in the region to help enhance PV systems.
- Further strengthen the development and dissemination of ICH guidelines in the field of PV and collaboration with WHO, contributing to the development of global PV standards.

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Annex 1. Building on the past: pharmacovigilance ecosystem overview

This annex provides an overview of key platforms, initiatives, tools and milestones that have shaped the global PV landscape over recent decades. It also illustrates the evolution of the PV ecosystem and the foundations on which the current strategy is built, emphasizing the importance of leveraging existing resources rather than duplicating efforts. While not intended to be exhaustive, this compilation offers historical context and reinforces the value of coordinated, system-based approaches to strengthening PV capacity.

Category	Stakeholders	References
Global networks and platforms	**WHO Programme for International Drug Monitoring** This platform was established after the WHA 16.36 resolution was adopted (Sixteenth World Health Assembly, 1963. The resolution was a result of the thalidomide tragedy that caused thousands of congenital deformations in infants due to in utero exposure during pregnancy. Around 87% of country and territories embers contribute to the WHO Global database of reported adverse events of medicinal products (VigiBase).	*(1,2)*
	The Global Vaccine Safety Blueprint (GVSB) This strategic document was developed by WHO and partners. It sets out indicators that aim to ensure that all countries have at least a minimal capacity to ensure vaccine safety. It was initially developed in 2011, and later updated in 2019 to align with Immunization Agenda 30.	*(3)*
	The Global Vaccine Safety Initiative (GVSI) This was set up to implement the Global Vaccine Safety Blueprint. It comprises a framework of eight strategic objectives aimed at enhancing global vaccine safety activities. The strategic objectives focus on building and supporting a systemic approach to vaccine PV in all LMICs.	*(4)*

Category	Stakeholders	References
	WHO Coalition of Interested Parties (CIP) This is a WHO-established network for regulatory systems strengthening. CIP promotes a unified strategic and coordinated approach to strengthening national and regional regulatory systems, to ultimately increase the effectiveness of collective efforts and to achieve the desired impact in countries and regions. CIP encompasses all regulatory functions, including pharmacovigilance, and ensures a comprehensive and coordinated approach to capacity building.	*(5)*
	WHO advisory groups Countries have access to international expertise and guidance in PV through the WHO Advisory Committee on Safety of Medicinal Products (ACSoMP) and the Global Advisory Committee on Vaccines safety (GACVS). The committees also inform public health policies with safety advice and risk analyses to disease treatment programmes, as well as the strategic advisory group of experts on immunization (SAGE), respectively.	*(6–8)*
	Global Vaccine Data Network (GVDN) Networks such as the GVDN have advanced the capacity of countries to conduct globally coordinated epidemiological studies on the safety and effectiveness of vaccines. The network shares common data protocols for observed over expected studies for adverse events of special interest (AESIs), rapid-cycle analyses, background rates of health outcomes of interest, and sentinel site surveillance studies.	*(9)*
Standardization of reporting and case definitions	**Standardization of reporting processes** using international guidance from technical and scientific platforms has allowed the development of standardized dictionaries (e.g. MedDRA), reporting tools (ICH E2B (R3), CIOMS reporting form, WHO recommended core variables) and methods (e.g. cohort event monitoring, CIOMS guide to vaccine safety surveillance, practical aspects of signal detection etc.).	*(10–12)*
	Standardized case definitions and guidelines for collecting and analysing AESI's have been developed by the Brighton Collaboration through extensive consultations with global experts. Projects such as the Global Alignment of Immunization Safety Assessment in Pregnancy (GAIA) have developed definitions for maternal and neonatal events.	*(13)*
	WHODrug Global is the international reference for medicinal product information maintained by the Uppsala Monitoring Centre (UMC). The dictionary is used to identify drug names and evaluate medicinal product information, including active ingredients and products' anatomical and therapeutic classifications, from nearly 150 countries.	*(14)*

Category	Stakeholders	References
Training and capacity building	The **WHO-ISOP PV Curriculum** is a structured competency-based framework that can be used by anyone who needs to plan and conduct PV training courses. It contains theoretical, comprehensive modular elements, practical tasks and key literature references and can be tailored to specific target audiences and levels of expertise and competency.	*(15,16)*
	The **Uppsala Monitoring Centre** offers both self-paced and instructor-led online courses structured around learning paths that delve into key PV concepts and processes. Advanced level learners have the possibility to take part in a face-to-face signal workshop held annually where they can investigate potential safety issues identified in their own national database. In addition, customized training is conducted with WHO, tailored to the needs of national safety surveillance programmes.	*(17)*
	Annual pharmacovigilance course for Francophone countries: The WHO Academy offers a wide range of courses for health professionals, policy-makers, and WHO staff, including several on pharmacovigilance. Examples of these courses are: Vaccine safety basics, AEFI causality assessment, Pharmacovigilance inspections and active surveillance.	*(18)*
Development of IT solutions	Development of IT solutions using standardized tools (e.g. VigiFlow, VigiMobile, Medsafety app, DHIS2, ODK app and others), has enabled their adoption in many countries, facilitating seamless electronic exchange of information.	*(17,19–21)*
Patient reporting	**The European region introduced patient reporting through new pharmacovigilance legislation**	*(22)*
	(Directive 2010/84/EC and European parliament and the council of the European), which enhances reporting, adding a new perspective contributing to better decision making in regulatory activities.	
	Many other countries have also adopted patient reporting.	
	The WHO guidance to PV centres on how to set up a patient reporting system has also been seminal in supporting these countries	*(23)*

Category	Stakeholders	References
PV methods to complement spontaneous reporting; integration of PV into public health programmes	Active surveillance has been used to monitor the safety of medicines for HIV, tuberculosis and malaria in many countries.	*(24,25)*
	WHO protocol templates for active surveillance, for example Cohort event monitoring for COVID-19 vaccines: The protocol template is for cohort event monitoring studies of COVID-19 vaccines but can be adapted to monitor adverse events of special interest for other medicines or vaccines groups (e.g. mpox vaccines in 2024).	*(26–28)*
	The African Leadership in Vaccinology Expertise (ALIVE) programme is a hospital-based sentinel surveillance system to detect safety signals of rare adverse events of special interest or to evaluate safety signals arising from other sources, following vaccination with COVID-19 vaccines. It was designed by the African COVID-19 Vaccine Safety Surveillance (ACVaSS) project in partnership with GVDN *(23)*, and was implemented in eight in African countries: Mali, Ghana, Nigeria, Ethiopia, Kenya, Malawi, Mozambique, Eswatini.	*(29,30)*
	WHO/UNICEF Joint Reporting Process: WHO and UNICEF jointly collect information through a standard questionnaire (the Joint Reporting Form) sent to all Member States. In 2021, this form was updated to a cloud-based solution known as the electronic Joint Reporting Form (eJRF). The eJRF collects countries' annual immunization data, which helps identify trends and gaps at the country, regional and global levels.	*(31)*
PV systems and functionality	**Minimum requirements of a basic pharmacovigilance system:** In 2010, the WHO and the Global Fund published the minimum pharmacovigilance requirement for countries applying to the Global Fund.	*(32)*
	WHO PV Indicators: A manual that provides a practical method for determining the PV indices. It can be used routinely by any worker in PV.	*(33)*
	WHO Global Benchmarking Tool is designed to evaluate the overarching regulatory framework and the component regulatory functions (e.g. clinical trial oversight) through a series of sub-indicators that may also be grouped and examined according to nine cross-cutting categories or themes, for example, quality and risk management system.	*(34)*
	UMC data mining methods for signal detection rely on a combination of computerized data mining and clinical evaluation of reports for the prioritization of medicine/vaccine–adverse effect combinations. In parallel, qualitative screening of scientific literature is conducted.	
	Causality assessment methods for ADR and AEFI: practical tools for the assessment of case reports.	*(35,36)*
	Tools for LMIC regulators for assessing risk management plans.	

Category	Stakeholders	References
Maternal and neonatal adverse events	**Landscape analysis of activities and data sources**	*(37)*
	The GAIA (**Global Alignment on Immunization Safety Assessment in Pregnancy**) consortium developed a set of standardized case definitions for AEFIs, specifically for maternal and neonatal outcomes, to create a common language for monitoring vaccine safety in pregnancy and improve data comparability across studies	*(38)*
	The **WHO Maternal and Neonatal Health Data Set** (mMNHDS) is a standardized set of core data elements used to collect information during and after pregnancy, at health facilities or obstetric and neonatal units, to diagnose outcomes according to standard definitions and ensure data comparability globally.	
	Study protocols: maternal and neonatal adverse events in pregnant people immunized with COVID-19 vaccines, WHO protocol on estimation of AESI background rates for neonatal outcomes.	*(39,40)*
Best practices	Good **reliance** practices.	*(40–42)*
	Good **regulatory** practices.	
	Good **vigilance** practices.	
Advocacy and communication	**MedSafety Week**: Since 2016, MedSafety Week has brought together PV and patient safety stakeholders around the world in a coordinated campaign to raise awareness and encourage the reporting of side-effects.	*(43)*
	Vaccine Safety Net is a global network of websites that provides reliable information on vaccine safety.	*(44)*

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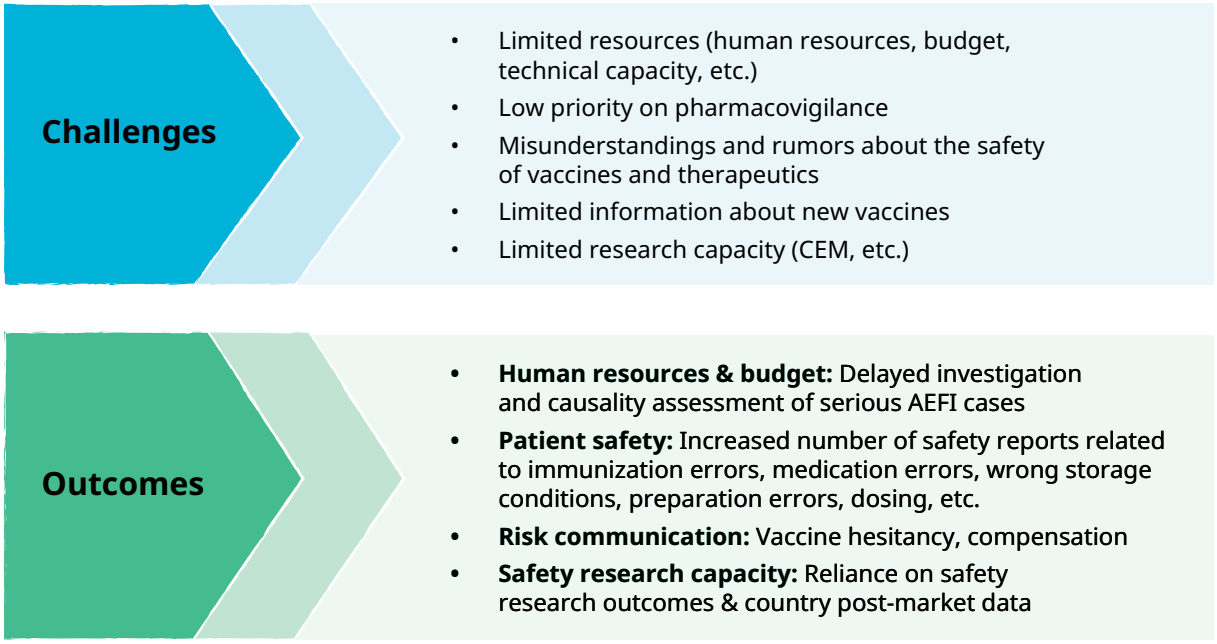
(All references were accessed on 20 October 2025).

Annex 2. Pandemic preparedness and pharmacovigilance

COVID-19 highlighted the serious gaps in the world's preparedness for pandemics and other health emergencies. While some countries were able to respond more effectively by rapidly leveraging existing preparedness plans and systems, the pandemic also exposed major weaknesses in PV capacity (Fig. A1). Many countries struggled with limited human resources, insufficient budgets, technical constraints, and restricted access to safety information on newly introduced vaccines. These challenges were compounded by the low priority often given to PV, underscoring the urgent need to strengthen PV systems as a core component of emergency preparedness and response.

Fig. A1. Pharmacovigilance results and effects during COVID-19 pandemic



The global smart pharmacovigilance strategy provides a framework to help countries respond more effectively to pandemics and other health emergencies. To implement this strategy successfully, it is essential to build on key lessons from COVID-19 responses, to enable timely and appropriate safety measures during the rollout of new medicines and vaccines:

- The COVID-19 pandemic offered valuable lessons, particularly through the **rapid development and emergency authorization of vaccines using novel platforms**.

These innovations present important opportunities for future preparedness. A notable success was the surge in spontaneous reporting, with over 0.5 million COVID-19 vaccine reports submitted to VigiBase – around 14% of all reports globally and 9% from LMICs. Understanding the factors behind this reporting surge is key to sustaining such momentum.

- **Global initiatives** such as access to COVID-19 tools and COVAX brought together governments, global health agencies, scientists, civil society and donors to accelerate equitable access to COVID-19 tools. Through a broad portfolio of vaccine candidates, the COVAX Facility enabled participating countries to access safe and effective vaccines. Collaborative efforts also extended to vaccine safety, with CEPI partnering with the Brighton Collaboration and the Task Force for Global Health to establish the SPEAC project. SPEAC supported harmonized safety assessments by developing definitions for adverse events of special interest, strengthening global capacity for coordinated vaccine monitoring.
- The GVDN and Gavi-supported African COVID-19 Vaccine Surveillance project successfully established hospital-based sentinel sites to detect AESIs across multiple African countries. These sites now offer a valuable foundation for future surveillance efforts. In parallel, reliance on emergency authorizations and WHO emergency use listings enabled LMICs with limited regulatory capacity to access COVID-19 vaccines. Post-market surveillance systems also proved critical, with timely signal detection – such as myocarditis linked to mRNA vaccines and TTS with the AstraZeneca vaccine – highlighting the importance of **sustainable safety infrastructure**.
- While COVID-19 revealed important gaps, it also reinforced the **value of reliance** as a core principle in global preparedness. Countries with limited capacity should be able to depend on decisions, safety data and regulatory assessments from trusted reference NRAs and mature surveillance systems. During the pandemic, data sharing and signal detection worked well in high-income countries, but safety data were limited for vaccines used primarily in LMICs. A strategic approach is needed to fill these gaps – one that encourages global data sharing, leverages existing infrastructures like sentinel sites, and prioritizes resource-intensive activities, such as active surveillance, in settings with stronger systems.

At different stages in a pandemic or health emergency, countries can use the WHO pharmacovigilance preparedness checklist in evolving ways to conduct gap analyses of their systems. A step-wise approach helps identify weaknesses in budget allocation, technical human resources, and overall pharmacovigilance capacity, enabling targeted improvements over time (Tables A1 to A3).

Table A1. PV system gap analysis at early stage of pandemic or health emergency

Country preparedness	• Conduct a gap analysis using the WHO Pharmacovigilance preparedness checklist • Allocate budget for AEFI investigations and causality assessments • Train additional human resources in adverse event reporting and investigation of serious cases • Provide training for causality assessment committees • Perform data analysis and studies on background rates of potential adverse events (e.g. annual myocarditis rates by age group) • Engage in reliance and work-sharing with other national regulatory authorities on risk management plans for new vaccines and medicines, safety information and data analysis
Expected challenges	• Difficulties in risk communication, including addressing rumours and misunderstandings about serious adverse events, and monitoring/responding to social media • Delays in serious AEFI investigations and causality assessments, affecting feedback to reporters and patients • Challenges in timely development of guidance and tools (e.g. CEM protocols) for active surveillance • Delays in safety report analysis for signal detection • Delayed access to updated regulatory safety information (e.g. updates to Patient Information Leaflets on identified adverse events)

During the peak pandemic stage, countries are encouraged to share real-time safety data to help detection of safety signals and better prepare for risk communication. Given the challenges with timely assessment of serious adverse events and potential safety signals in resource-limited settings, countries are encouraged to rely on the safety information updates from high-income countries to take timely regulatory actions.

Table A2. PV system gap analysis at peak stage of pandemic or health emergency

Country preparedness	• When new medicines and vaccines become available, review and use risk management plan • Ensure early detection of potential safety signals and sharing with global stakeholders • Allocate budget for investigation of serious adverse events and causality assessments • Support transparent and well-structured risk communication
Expected challenges	• Timely review of potential safety signals • Structured risk communication responses and related support • Timely assessments and verification of potential safety signals

During the post-pandemic stage, countries can review areas for further improvement and continue addressing gaps to strengthen the PV system.

Table A3. PV system gap analysis at post-pandemic stage

Country preparedness	• Review areas for improvements • Continue addressing IDPs to strengthen PV systems • Keep the momentum of meeting AEFI performance indicator • Identify stakeholders for data sharing and reliance
Expected challenges	• Continue monitoring of safety signals and long-term effects • Assessment of pandemic response • Revisit the lessons learned • Develop PV preparedness packages for the next pandemic

Annex 3. Key institutions supporting implementation of *The global smart pharmacovigilance strategy*

This annex profiles selected organizations playing a strategic role in supporting the implementation of *The global smart pharmacovigilance strategy*. These institutions contribute through technical expertise, capacity building, collaborative regulatory support, and global or regional coordination. While not exhaustive, the examples included here illustrate the range of partnerships and mechanisms that help strengthen PV systems, particularly in LMICs, and advance shared goals such as reliance, work-sharing, and risk-informed prioritization.

Uppsala Monitoring Centre (UMC)

A non-profit foundation established in 1978 through an agreement between the WHO and the Government of Sweden for the operations of the WHO PIDM *(1)*. To date, UMC continues to support PIDM members by working towards safer use of medicines and vaccines. UMC supports PV implementation by focussing on prioritization, promoting the concept of reliance, work sharing and risk communication.

UMC prioritizes signal investigations and works closely with WHO to provide signal detection and validation support to WHO disease and immunization programmes, the WHO global advisory groups on the safety of medicines and vaccines. UMC publishes signal documents and distributes this routinely to PV centres supporting risk communication at a national level. By contributing data to VigiBase, the WHO database of adverse event reports for medicines and vaccines, PIDM members are already applying the concept of work-sharing by pooling safety data. This can strengthen signal detection capabilities. Increasing the reporting frequency and quality and timeliness of reporting is essential for future global signal monitoring. Going forward, UMC will strive for enhanced VigiBase contributions from WHO PIDM members and promote the use of the global data source. UMC continues to actively participate in regional working groups, meetings and events to foster collaboration and address regional PV needs effectively and host regular information-sharing sessions.

UMC support overall regulatory system strengthening by helping to fill gaps in their institutional development plans for PV in collaboration with WHO and other stakeholders. UMC has a long-standing history of offering diverse PV learning programmes and resources. UMC will continue to support capacity building with a streamlined educational offering ensuring excellent support for PIDM members.

Training is available in relevant languages and meets the needs of diverse user groups through collaboration and new technology. UMC seeks to further develop and enhance data collection and management of adverse event reports to meet the specific needs of these stakeholders.

International Society of Pharmacovigilance (ISoP)

A global professional organization dedicated to advancing PV science and practice, playing an important role in supporting the implementation of *The global smart pharmacovigilance strategy* as a member of the WHO Coalition of Interested Parties (CIP). ISoP has a strong history of collaboration with WHO for developing training materials that align with international standards while being practical for real-world use and building capacity *(2)*.

Through its network of over 1300 members, the society fosters global collaboration and knowledge sharing from a diverse range of organizations, disciplines and backgrounds, including regulatory authorities, academic institutions, pharmaceutical companies, and health care organizations in over 100 countries. This diverse expertise allows ISoP to provide specialized knowledge for different aspects of safety monitoring of health care products.

ISoP supports the implementation of the WHO strategy by utilizing its:

- 10 regional chapters that provide region-specific insights and platforms for discussion, helping to advance pharmacovigilance efforts;
- 14 Special Interest Groups, which invite people from different countries to join, discuss and create strategies for addressing specific challenges;
- ISoP Communities, such as fellows, students and honourary members, which create an environment of sharing and building knowledge in PV; and,
- alliances with global organizations such as the International Medication Safety Network, CIOMS, International Ergonomics Association, UMC and others.

In addition, as part of its core mission ISoP is promoting PV knowledge through:

1. Special projects of research: Including collaboration with WHO to develop and disseminate the global PV curriculum, tailored to scientific advances and regional needs. This serves as the foundation for all training.
2. Training activities: Delivered through annual and mid-year meetings, chapter events, SIG meetings and courses, and integrated with global PV training initiatives. These efforts focus on building capacity among regulatory agencies and other key stakeholders.
3. Global PV professional certification: Available to individuals working in regulatory authorities and other government bodies involved in pharmacovigilance.

Paul-Ehrlich-Institut

The Paul-Ehrlich-Institut (PEI) is the Federal Institute for Vaccines and Biomedicines in Germany and the EU. As a CIP member, the institute provides region-specific support to WHO in building PV systems in LMICs in Africa *(3)*. This activity is part of the Global Health Protection Program supported by the German Ministry of Health *(4)*.

The institute envisages supporting implementation of *The global smart pharmacovigilance strategy* by supporting the following areas:

- Strengthening of regulatory systems in African Member States.
- Capacity building activities at the individual and national levels.
- Harmonization of regulatory frameworks.
- Facilitating cooperation between key organizations within the African continent.

Through a seven-year collaboration, PV systems were enhanced in The Gambia, Liberia, and Sierra Leone. Zimbabwe's MCAZ reached maturity level (ML) 3, and Ghana's FDA achieved ML4 in 2024, based on WHO benchmarking. These results were achieved by updating regulatory frameworks and procedures in line with countries' IDPs. PEI also provided targeted training – including workshops and train-the-trainer programmes – on adverse drug reaction reporting, causality assessment, signal management, periodic safety updates, and benefit–risk assessment. Joint inspections further promoted work-sharing and reliance. PEI is now extending this support to Senegal and Rwanda under the WHO CIP-coordinated procedure and will continue to assist Member States in line with their IDPs and the CIP roadmap.

Beyond individual country support, PEI contributes to regional harmonization by working with African Union Development Agency-NEPAD to implement the Vigilance Technical Committee and African Vaccine Regulatory Forum (AVAREF) roadmaps. This collaboration has led to the development and roll out of standardized templates and guidelines for vaccine safety assessment during the pre-authorization phase, with implementation supported through AVAREF-led workshops.

At the global level, PEI contributes to regulatory networks. As a WHO Collaborating Centre for the Standardization and Evaluation of Vaccines, PEI helps develop and implement WHO guidelines on scientific vaccine assessment, supporting the *Global Vaccine Action Plan*.

PEI also provides technical support to WHO in developing advanced tools for investigating adverse events following immunization, causality and risk assessment, and analysis of vaccine-preventable disease epidemiology. It will continue helping Member States adapt and apply these tools to enhance their readiness for safety monitoring and risk management of medicines and vaccines.

PEI remains committed to supporting implementation of *The global smart pharmacovigilance strategy* through capacity building, knowledge transfer, promotion of work-sharing and reliance, and ongoing advancement of national regulatory systems – both in Africa and globally.

The WHO Collaborating Centre for Pharmacovigilance in Public Health Programmes and Regulatory Services

The Indian Pharmacopoeia Commission (IPC), an autonomous institution under the Ministry of Health and Family Welfare of the Government of India, has been operational since 2009, with the mandate to promote and monitor the safety and quality of medical products in India. The National Coordination Centre of the Pharmacovigilance Programme of India (NCC-PvPI) was initiated in 2010 and subsequently integrated into the IPC in 2011 *(5)*.

In October 2017, NCC-PvPI was designated as a WHO Collaborating Centre for Pharmacovigilance in Public Health Programmes and regulatory services with the following key terms of reference:

- Support WHO in the creation of relevant tools and guidelines for enhancing PV practice in LMICs in Asia and beyond.
- Contribute to WHO efforts to build capacity of WHO Member States to establish high quality PV systems for medical products, including medical devices.
- Support WHO by providing technical guidance to support the integration of PV within public health programmes (e.g. tuberculosis, neglected tropical diseases, vector-borne diseases, HIV/AIDS, immunization) and regulatory issues.

The Centre applies the principles of *The global smart pharmacovigilance strategy* in implementing its workplan. For example:

- helping to prepare a list of 75 medicines used in countries in the region that are to be prioritized for signal detection and review;
- advancing reporting harmonization in the region by mapping ADR reporting forms to WHO-identified core variables as a part of the WHO SEARN;
- developing a quarterly SEARN newsletter, promoting mutual reliance and information exchange among the members.

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Annex 4. Approach to content development

The conceptualization of this strategy began late 2019, to implement the recommendations from the 2018 International Conference of Drug Regulatory Authorities and building on the lessons learned from the WHO Smart Safety Surveillance (3S) pilot project that was conducted in collaboration with the Bill and Melinda Gates Foundation in the preceding years. The initial draft was subsequently expanded to incorporate broader vaccine safety principles, embrace concepts of regulatory system strengthening, reliance and, work-sharing and integrate insights gained during the COVID-19 pandemic.

Building on this groundwork, the current document was developed through a comprehensive and consultative process, drawing input from global, regional, and country levels, including key external stakeholders. A core team of pharmacovigilance experts at WHO headquarters initiated the process by reviewing existing normative documents, including the WHO Global vaccine safety blueprint 2.0 and the 3S approach. Key principles were combined into a single strategic framework with proposed guidance on implementation.

The draft was circulated to WHO regional offices and the WHO Collaborating Centre for International Drug Monitoring (Uppsala Monitoring Centre) for initial feedback. Regional offices identified countries with relevant case studies, which were invited to contribute written examples. These case studies were integrated into the document to illustrate the real-world application of the strategic principles.

In August 2024, stakeholders including the Bill & Melinda Gates Foundation, United States Centers for Disease Control and Prevention (US CDC), the Global Fund, UNITAID, United Nations Development Programme (UNDP), GAVI and United Nations Children's Fund (UNICEF) were invited to provide feedback. Responses were received from the Global Fund and US CDC, and their comments were reviewed and incorporated. The strategy was then presented at a WHO Pharmacovigilance Partners Meeting, held on 13 October 2024 in New Delhi, attended by 148 regulators, national medicines or vaccines safety focal points from 68 countries, and representatives from WHO Collaborating Centres and international organizations including African Union Development Agency – New Partnership for Africa's Development (AUDA NEPAD), Bill and Melinda Gates Foundation, Council for International Organizations of Medical Sciences (CIOMS), International Clinical Epidemiology Network (INCLEN), Global Vaccine Data Network, Safety Platform for Emergency Vaccines (SPEAC) and Uppsala Monitoring Centre (UMC). The draft strategy was also presented at the joint meeting of the WHO Advisory Committee on Safety of Medicinal Products (ACSoMP) and the Global Advisory Committee on Vaccine Safety (GACVS) in November 2024. Key discussion points and recommendations from these meetings were incorporated into the final draft.

Following these extensive consultations, the final version of the document was prepared and shared with all contributors for review and approval, ensuring consensus and collective ownership of the final product.

In accordance with the WHO policy on declaration of interest by WHO experts, all external contributors from non-state actors involved in the development of this document, including representatives from UMC, CIOMS, INCLEN, Global Fund, and committee members of ACSoMP and GACVS, submitted declaration of interest forms. The WHO Secretariat reviewed each submitted declaration. Following this review, it was concluded that none of the external contributors had any potential or reasonably perceived conflicts of interest related to the subject matter of this document.

WHO internal funds were used for the overall development of this strategy.