Emerging trends in pharmacovigilance: global surveillance systems, signal detection, risk assessment and patient safety

Amit Chawla[*1], Pradeep Balakrishnan[2], Sahil Thakral[3], Payal Rani[4], Lovesampuranjot Kaur[5]

*[*1]Professor Cum Principal, Faculty of Pharmacy, Tantia University, Sri Ganganagar, Rajasthan, India*

[2]Lecturer, School of Integrative Medicine and Life Sciences, KPJ Healthcare University, Malaysia

[3]Assistant Professor, Department of Forensic Medicine and Toxicology, Dr. S. S. Tantia Medical College, Hospital and Research Centre

[4]Professor Cum Principal, Mata Jarnail Kaur Memorial College of Pharmacy (Under Desh Bhagat University), Sri Muktsar Sahib, Punjab, India

[5]Principal, Faculty of Nursing, Desh Bhagat University, Mandi Gobindgarh

DOI: 10.5281/zenodo.23880628

Abstract:

Pharmacovigilance has evolved from a system based mainly on spontaneous adverse drug reaction reporting into a multidimensional discipline that combines global case-report databases, active surveillance, pharmacoepidemiology, digital health records, patient-generated information and advanced analytics. This expansion is necessary because pre-authorisation trials cannot fully identify rare, delayed, interaction-related or population-specific harms that emerge during routine use. This narrative review examines the architecture of international pharmacovigilance, major surveillance platforms, signal-detection approaches, clinical and regulatory risk assessment, and current developments in artificial intelligence and real-world evidence. The World Health Organization Programme for International Drug Monitoring and VigiBase provide a framework for cross-national learning, while regional and national systems such as EudraVigilance, the United States Food and Drug Administration Adverse Event Reporting System and India's Pharmacovigilance Programme of India support local reporting and regulatory action. Disproportionality methods, including the reporting odds ratio, proportional reporting ratio, information component and empirical Bayes approaches, are useful screening tools but do not establish causality or incidence. Active surveillance and well-designed non-interventional studies can strengthen signal evaluation by supplying denominators, comparators and longitudinal outcomes. Artificial intelligence can assist case processing, coding, duplicate detection and pattern recognition; however, biased data, limited external validation, weak explainability and automation errors require human oversight. Recent ICH E2D (R1) and M14 guidance further emphasise fit-for-purpose safety data and harmonised study methods. The review concludes that effective pharmacovigilance depends not on data volume alone but on reliable reporting, transparent analysis, timely risk communication, equitable global participation and practical measures that improve patient outcomes.

Keywords:

pharmacovigilance; adverse drug reactions; global surveillance; VigiBase; EudraVigilance; FAERS; signal detection; real-world evidence; artificial intelligence; patient safety.

1. Introduction:

Medicines are central to the prevention and treatment of disease, but no medicinal product is entirely free from risk. An adverse drug reaction (ADR) is a harmful or unintended response associated with the use of a medicinal product. In routine clinical practice, the term adverse event is broader: it describes an unfavourable medical occurrence after exposure, whether or not a causal relationship has been established. This distinction

is important because pharmacovigilance begins with suspicion and evidence gathering; it does not assume that every event reported after treatment was caused by the medicine (Edwards and Aronson, 2000).

Pre-marketing clinical trials are essential for establishing efficacy and identifying common short-term adverse effects. Nevertheless, trial participants are often selected, follow-up is limited, and sample sizes may be insufficient to identify uncommon events. Patients with multiple diseases, older adults, pregnant people, children and those receiving many medicines may be under-represented. A rare event occurring in one patient per several thousand exposures may remain undetected until a medicine is used by a much larger population. Delayed toxicity, cumulative exposure, interactions and medication-use errors may also become apparent only after widespread use.

Pharmacovigilance is defined by the World Health Organization (WHO) as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or other medicine-related problems. Its purpose is broader than collecting reports. It aims to maintain a favourable benefit-risk balance throughout the product life cycle, support safe use, identify preventable harm and communicate practical advice to patients and health professionals (WHO, 2026).

The discipline is now being reshaped by connected global databases, electronic individual case safety reports (ICSRs), active surveillance networks, real-world data, patient reporting, natural language processing and machine learning. At the same time, the growing volume and variety of data create challenges involving data quality, duplicates, reporting bias, privacy, interoperability and the interpretation of statistical associations. This review describes how these components fit together and why strong clinical judgement and regulatory governance remain essential.

2. Review approach and scope:

This article is a narrative review, not a systematic review or meta-analysis. It synthesises major international guidance, regulatory resources and selected peer-reviewed publications relevant to global surveillance systems, signal detection, risk assessment, emerging digital methods and patient safety. Sources were selected for their relevance to established pharmacovigilance principles and developments available up to 31 October 2026. Particular attention was given to WHO resources, European Medicines Agency (EMA) good pharmacovigilance practices, United States FDA systems, Indian PvPI, and the ICH E2D (R1) and M14 guidelines. The discussion is intended to explain core concepts and emerging directions rather than provide a complete country-by-country inventory of reporting laws.

3. Evolution and scope of modern pharmacovigilance:

The modern international framework developed after serious medicine-related safety events demonstrated that isolated national reporting systems could not adequately identify risks shared across borders. The WHO Programme for International Drug Monitoring (PIDM) was established in 1968 to facilitate international collaboration and exchange of suspected ADR reports. Member countries contribute ICSRs to VigiBase, the WHO global database maintained by the Uppsala Monitoring Centre (UMC). WHO describes the database as containing reports submitted by participating national centres, allowing signals to be explored across products, events and populations (WHO, 2026). As of July 2026, the WHO PIDM included 162 full members and 20 associate members. WHO reported that VigiBase contained more than 35 million reports in July 2023; this figure is a dated indicator of scale rather than a live database count. The database is a collective resource: its value depends on the completeness and quality of reports contributed by participating national centres.

The scope of pharmacovigilance has also expanded beyond conventional prescription medicines. Monitoring may include vaccines, biological products, blood products, herbal and traditional medicines, medical devices, combination products and products used in public health programmes. Relevant problems include suspected ADRs, lack of therapeutic effect, medication errors, overdose, misuse, abuse, dependence, interactions, product defects, substandard or falsified products and problems associated with medication-use processes. These areas may have different reporting routes and regulatory definitions, but they share the goal of identifying and reducing preventable harm.

A life-cycle approach is now expected. Safety information is assessed during clinical development, at authorisation, after launch and throughout the period in which a product remains in use. The safety profile may change when the medicine is prescribed to new populations, used for new indications, combined with other therapies or supplied through different healthcare systems. Pharmacovigilance therefore requires an ongoing cycle of collection, analysis, evaluation, action and follow-up rather than a one-time assessment (WHO, 2026).

4. Global surveillance systems and data infrastructure:

Global pharmacovigilance depends on national centres, regional regulators, manufacturers, healthcare institutions, patients and international organisations. These actors operate different but interconnected systems. The main platforms vary in their legal scope, data sources, access arrangements and analytical functions. They should not be viewed as interchangeable databases: a spontaneous-reporting system is designed primarily to collect suspected cases, whereas an active surveillance network can analyse defined populations and estimate rates when appropriate denominators and valid outcome definitions are available.

Table. 1: Global surveillance systems and data infrastructure

System or network	Main function and data contribution	Important interpretation point
WHO PIDM / VigiBase	International repository of ICSRs submitted by national pharmacovigilance centres; supports global signal exploration and cross-country learning.	Reports are suspected associations; reporting volume is not an incidence denominator.
EudraVigilance	EU/EEA system for electronic exchange and analysis of suspected adverse reactions from clinical trials and post-authorisation use.	Public reports are restricted and aggregated; a report does not prove causation.
FDA FAERS / MedWatch	US post-marketing reports of adverse events and medication errors involving drugs and therapeutic biologics; supports safety surveillance.	Duplicates, stimulated reporting and incomplete exposure data limit rate calculations.
FDA Sentinel	Active surveillance using routinely collected healthcare data in a distributed network; supports targeted safety studies.	Claims and EHR data have coding, capture and confounding limitations; study design is essential.
India PvPI	National programme coordinated by the Indian Pharmacopoeia Commission; receives reports through ADR Monitoring Centres and patient/HCP channels.	National reporting quality and timely clinical follow-up determine signal usefulness.

5. WHO Programme for International Drug Monitoring and VigiBase:

The WHO PIDM provides a common international framework for national pharmacovigilance centres to submit suspected reactions in a standardised format. VigiBase supports large-scale data mining and comparison of reporting patterns across medicines, events, age groups, sex and geographical regions. The UMC provides technical support and training to national centres. These services help strengthen case management and signal analysis using international standards (WHO, 2026).

The international database is especially useful when a suspected reaction is rare, reported in several countries or associated with a newly introduced product. A signal may become visible in pooled data before any single country has enough reports to recognise a pattern. However, international pooling can also combine reports generated under different prescribing patterns, healthcare access, reporting cultures and regulatory requirements. Analysts must therefore consider country, time, indication, age, sex, co-medication and other relevant factors when interpreting an apparent association.

5.1. Eudravigilance in the European Union:

EudraVigilance is the EMA-managed system for collecting and analysing suspected adverse reaction reports related to medicines authorised or studied in the European Economic Area. It supports electronic exchange of ICSRs among EMA, national competent authorities, marketing authorisation holders and clinical-trial sponsors. It also supports signal detection and the improvement of product information. The database includes reports from spontaneous sources, post-authorisation studies and relevant scientific literature, as well as suspected unexpected serious adverse reactions from clinical trials (EMA, 2026).

The EU makes selected EudraVigilance information publicly accessible through the adrreports.eu portal. These data are intended to promote transparency and permit exploration of suspected side effects. EMA explicitly cautions that reports describe events observed after exposure and do not, by themselves, demonstrate that a medicine caused the event. Interpretation requires review of the clinical case details and all other available evidence (EMA, 2026).

5.2. United States: FAERS, MedWatch and Sentinel:

The FDA Adverse Event Reporting System (FAERS) contains adverse event and medication-error reports submitted to FDA for approved drugs and therapeutic biological products. Reports may originate from consumers, healthcare professionals and manufacturers. FAERS supports post-marketing safety surveillance and is structured to use international reporting standards and MedDRA terminology. Public data can help researchers identify reporting patterns, but the database is not designed to calculate the incidence of adverse reactions because the number of exposed patients, completeness of reporting and duplication status are not fully known (FDA, 2026).

MedWatch is the FDA safety information and reporting programme for health professionals and the public. Spontaneous reporting is complemented by the FDA Sentinel System, which uses routinely collected healthcare data and distributed analytical tools to investigate defined safety questions. The FDA Office of Surveillance and Epidemiology reported that the Sentinel Distributed Database contained over 1.5 billion person-years of data and more than 541 million unique patient identifiers as of 2025. Such scale creates opportunities for rapid, population-based analyses, although the suitability of the data still depends on whether exposure, outcomes and potential confounders are captured accurately (FDA, 2025; Taherifard et al., 2026).

5.3. Pharmacovigilance Programme of India:

The Pharmacovigilance Programme of India (PvPI) was initiated in 2010 under the Central Drugs Standard Control Organisation, with the national coordinating centre later transferred to the Indian Pharmacopoeia Commission (IPC), Ghaziabad. The programme collects, collates and evaluates suspected ADR reports through ADR Monitoring Centres (AMCs), with reporting routes available to healthcare professionals and patients. Its purpose is to improve the safety of medicines used in the Indian population and provide evidence for regulatory decisions and risk communication (Indian Pharmacopoeia Commission, 2025).

India has a particularly important need for strong pharmacovigilance because of its large and diverse population, wide range of public and private healthcare settings, substantial use of generic medicines, variable access to diagnostic services and extensive use of traditional and herbal products. Reporting forms in multiple Indian languages and access for patients can reduce barriers. Hospital pharmacists, nurses, physicians and pharmacology departments can strengthen the programme by recognising suspected reactions, documenting relevant clinical details, reporting promptly and participating in follow-up. A national system is only as useful as the quality and representativeness of the reports it receives.

6. Data sources and quality in contemporary surveillance:

Spontaneous reporting remains a foundation of pharmacovigilance because it can capture unexpected events from everyday practice without requiring a formal study. A report generally includes details of the patient, suspected medicine, event, reporter, dates, outcome, medical history and concomitant treatment. The four minimum elements used to identify a valid ICSR are an identifiable patient, an identifiable reporter, a suspected medicinal product and a suspected adverse reaction. Identifiability does not require publishing a person's name; it means that the case can be distinguished and followed up under applicable privacy requirements.

Other sources include clinical trials, observational studies, electronic health records, insurance claims, disease and product registries, poison-centre data, medication-error reports, published literature, patient-support programmes and selected digital platforms. Each source has different strengths. Spontaneous reports can be timely and useful for novel events, while EHRs may provide laboratory results, diagnoses and clinical narratives. Claims data can support large longitudinal studies but may lack clinical detail. Registries can provide well-defined populations, and patient-generated information may reveal effects that are difficult to capture during short clinical encounters.

Data quality is not simply a matter of report count. Complete dates, dose, route, indication, treatment duration, co-medications, relevant history, laboratory values, treatment changes and clinical outcomes improve assessment. Clear descriptions help medical reviewers distinguish a suspected reaction from disease progression, infection, treatment failure or an unrelated event. Follow-up should be prioritised for serious, unexpected, medically important or poorly documented cases. Duplicate detection is also essential because the same event may be reported by a patient, clinician and manufacturer or appear in multiple databases.

Under-reporting is a longstanding limitation of spontaneous systems. Healthcare professionals may be uncertain about causality, lack time, forget to report, and believe that only serious or proven reactions qualify, or receive little feedback after submitting a report. Patients may not recognise a symptom as medicine-related or may face language and digital-access barriers. Hazell and Shakir (2006) demonstrated substantial under-reporting across the studies they reviewed, although the degree varied by setting and method. Under-reporting means that absence of reports should never be interpreted as proof that a product is safe.

Reporting can also be stimulated by media attention, regulatory warnings, new product launches, and litigation or public health campaigns. This may cause a temporary increase in reports without a corresponding increase in the underlying event rate. Conversely, changes in medicine use, market share, reporting rules and public awareness can alter reporting patterns over time. Analysts need to consider these influences when comparing products, countries or periods.

6.1. Signal detection: from clinical observation to statistical screening:

A safety signal is information from one or more sources that suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event that warrants further investigation. A signal is not a confirmed adverse reaction. It is a reason to evaluate evidence. Signals may arise from an individual well-documented case, a cluster of cases, a clinical trial imbalance, a spontaneous database pattern, an observational study, a literature report or a combination of sources (EMA, 2017; CIOMS, 2010).

Traditional signal detection begins with clinical review. Reviewers assess the timing of exposure and event, biological plausibility, dechallenge and rechallenge information, dose relationship, alternative causes, known pharmacology, laboratory findings and the consistency of similar reports. A detailed case may be important even when only one or two reports exist, particularly when the event is rare, serious, distinctive and temporally plausible. Statistical methods can identify patterns in large datasets, but they cannot replace the clinical interpretation of individual cases.

6.2. Quantitative disproportionality methods:

Disproportionality analysis compares the proportion of a particular event reported for one medicine with the proportion reported for other medicines in the same database. Common measures include the reporting odds ratio (ROR), proportional reporting ratio (PRR), Bayesian information component (IC) and empirical Bayes geometric mean (EBGM). These methods screen for unusually frequent co-reporting and help prioritise combinations for review (Bate and Evans, 2009).

The ROR compares the odds of a specific event being reported rather than another event for a medicine versus other medicines. The PRR compares the proportion of reports containing the event for the medicine with the corresponding proportion for the comparator set. Bayesian methods, including the information component and empirical Bayes approaches, use statistical shrinkage to reduce the influence of unstable estimates generated by very small counts. Each method has different assumptions, thresholds and sensitivity to sparse data. No single algorithm is optimal for every product, event or database.

Disproportionality is not a measure of incidence, absolute risk or relative risk in the epidemiological sense. The underlying database generally lacks a reliable denominator of all exposed patients and is influenced by selective reporting. A high ROR or PRR does not prove that the medicine caused the reaction, and a low value does not exclude a genuine risk. Confounding by indication, co-medication, notoriety bias, channeling of higher-risk patients to particular treatments and differential reporting can all produce or mask an apparent signal. Bate and Evans (2009) and CIOMS (2010) emphasise that statistical outputs require contextual assessment and should be used as screening tools.

Table. 2: Quantitative disproportionality methods

Method	What it contributes	Main caution
ROR / PRR	Frequentist measures of disproportionate reporting; relatively transparent and computationally simple.	Can be unstable with small counts and affected by reporting bias and confounding.
Information component (IC)	Bayesian information-theoretic measure; shrinkage helps moderate sparse-data effects.	Requires appropriate interpretation of posterior estimates and thresholds.
EBGM	Empirical Bayes estimate that stabilises observed-to-expected reporting patterns.	Model assumptions and database characteristics affect performance.
Clinical review	Assesses chronology, plausibility, competing explanations and seriousness.	Time-intensive; reviewer expertise and case completeness matter.
Active surveillance	Uses defined populations and comparators to evaluate risk more directly.	Needs fit-for-purpose data, valid outcome definitions and control of bias.

6.3. Data mining, pattern recognition and temporal analysis:

Large databases permit more than pairwise drug-event screening. Data-mining approaches can examine combinations, event sequences, co-medication patterns, age-specific effects and changes in reporting over

time. Temporal methods may help identify whether a signal is increasing, stable or declining. Stratified analysis can reveal a signal concentrated in a particular subgroup, although excessive subgroup testing can increase false-positive findings. (Harpaz et al., 2012) described how data-mining methods can support adverse-event discovery and analysis across several pharmacovigilance data types.

Signal detection programmes should be designed around the product's known and potential risks, not solely around automated statistical thresholds. A useful strategy combines routine screening, targeted monitoring of important risks, clinical review of serious case reports, periodic reassessment of known events and review of external evidence. Thresholds should be documented, applied consistently and interpreted alongside the number of reports, case quality, novelty, severity, plausibility and public health importance.

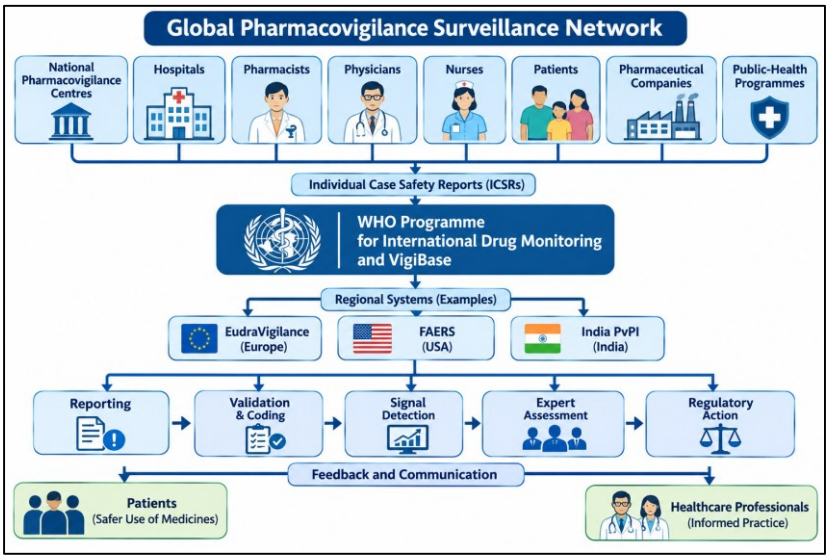


Figure. 1: Global Pharmacovigilance Surveillance Network: International Reporting Systems, VigiBase, Signal Detection, Regulatory Action and Feedback for Medicine Safety

6.4. Emerging digital approaches and artificial intelligence:

The growth of electronic health records, digital reporting portals, patient-support programmes and large spontaneous-reporting databases has increased the volume of information that must be processed. Artificial intelligence (AI), machine learning (ML) and natural language processing (NLP) are being explored to support case intake, extraction of drug and event names, coding, duplicate detection, triage, literature monitoring and signal prioritisation. These tools may reduce repetitive work and help reviewers focus on clinically complex cases.

NLP can convert narrative text into structured information. For example, a patient note may state that a medicine was stopped after a rash developed and that the rash improved several days later. An NLP system may identify the medicine, event, chronology and dechallenge information, then suggest standardised terminology for human confirmation. Transformer-based language models can assist with extracting relationships from clinical narratives, while rules-based methods remain useful for predictable tasks such as checking missing fields or formatting data. (Li et al., 2024) reviewed machine- and deep-learning approaches for adverse drug event extraction from clinical text, describing strengths and limitations across benchmark datasets.

Machine-learning models can also screen for unusual patterns that are difficult to identify through simple pairwise comparisons. Algorithms such as random forests, gradient boosting and neural networks may combine medicine, event, patient and temporal features. However, model performance can be overstated when testing uses the same source population, labels or time period used in model development. A model may learn reporting behaviour or the popularity of a medicine rather than a clinically meaningful biological association. Performance should therefore be assessed using external datasets, appropriate reference standards, calibration, sensitivity, precision, subgroup fairness and prospective workflow evaluation.

(Warner et al., 2025) described opportunities for AI in pharmacovigilance signal management while emphasising the need to maintain appropriate scientific and governance controls. A systematic review published in 2026 similarly found growing use of AI/ML across signal detection, adverse-effect prediction and case processing, but highlighted limited external validation and few prospective implementation studies (El Sayed et al., 2026). These findings support a cautious approach: AI can prioritise and organise evidence, but

should not independently confirm causality, make treatment decisions or issue regulatory conclusions without accountable human review.

Important risks include hallucinated or incorrectly extracted details, missed negation, confusion between current and historical medicines, poor performance on abbreviations, language-related bias, over-representation of certain populations, cybersecurity threats and leakage of identifiable health information. Generative AI systems may produce plausible but unsupported summaries unless the source text and extracted facts are traceable. Any deployed model should have version control, audit trails, access control, documented intended use, monitoring for drift, validation on local data and a clear escalation route for uncertain cases.

7. Real-world data and active surveillance:

Real-world data (RWD) include information collected during routine healthcare, such as electronic health records, administrative claims, registries, laboratory systems, prescription records and patient-generated data. When appropriately analysed, these sources may produce real-world evidence (RWE) about medicine safety in populations and circumstances that are not fully represented in clinical trials. Unlike spontaneous reports, many RWD studies can define a source population, exposure period, and comparator group and outcome ascertainment method. They may therefore estimate event rates and relative measures when the data are fit for the research question.

Active surveillance can be particularly useful for evaluating a signal that has emerged from spontaneous reports. A cohort study may compare new users of a medicine with users of an appropriate alternative treatment. A self-controlled design may compare risk periods within the same patient. A case-control study may evaluate exposure among people with and without a defined outcome. Each design has specific assumptions and possible biases. Important issues include confounding by indication, immortal-time bias, exposure misclassification, outcome misclassification, missing data, incomplete capture of over-the-counter medicines and differences in healthcare-seeking behaviour.

The ICH M14 guideline, finalised in 2025 and implemented through regional guidance including FDA final guidance in March 2026, sets harmonised principles for planning, designing, analysing and reporting non-interventional studies using RWD for medicine safety assessment. It emphasises a clearly defined research question, assessment of data fitness-for-use, feasibility assessment, transparent definitions of exposure and outcomes, pre-specified analysis and clear reporting of limitations (ICH, 2025; FDA, 2026). M14 is important because it encourages regulators and sponsors to use consistent, transparent methods rather than assuming that any large database automatically produces reliable evidence.

The FDA Sentinel System illustrates a distributed active-surveillance model. Rather than requiring all identifiable patient records to be centralised, participating organisations can run harmonised queries against local data using a common data model. This approach can support large-scale analyses while retaining data partner control over patient-level information. It is not a universal solution: some safety questions cannot be answered if outcomes are not coded reliably, clinical details are absent or the exposure group is too small. Recent assessment of Sentinel has highlighted both its regulatory value and the importance of transparent study documentation and fit-for-purpose data (Taherifard et al., 2026).

8. Clinical risk assessment and benefit-risk evaluation:

After a signal is identified, the next task is to determine whether it represents a credible safety concern and what action, if any, is required. Risk assessment integrates clinical case review, epidemiology, pharmacology, toxicology, product quality, exposure estimates, background disease rates and the consequences of treatment alternatives. It considers the seriousness of the outcome, its expectedness, severity, reversibility, preventability, time to onset, dose relationship and the characteristics of affected patients. A rare but life-threatening event may require a different response from a common, mild and reversible adverse effect.

Causality assessment asks whether the medicine could reasonably have contributed to the event. Chronology is essential: an event that began before exposure is unlikely to have been caused by the medicine, although treatment may worsen it. Dechallenge information may support causality if the event improves after withdrawal, while rechallenge can provide useful evidence but may be unsafe or unethical when the suspected reaction is serious. Alternative explanations, including the underlying disease, infection, other medicines and diagnostic error, must be considered. Structured tools such as the WHO-UMC system or Naranjo algorithm can improve consistency, but neither should be applied mechanically or treated as a substitute for expert judgement.

Risk assessment also distinguishes hazard from risk. A hazard is the potential of a medicine to cause harm; risk considers the likelihood and consequences of that harm under actual conditions of use. The same adverse effect may have different implications depending on its frequency, severity, the indication, baseline disease

risk, availability of alternatives and the benefit obtained. For a medicine treating a life-threatening condition with few alternatives, a manageable serious risk may be acceptable with appropriate controls. For a medicine used for a minor condition, a similar risk may shift the balance towards restriction or withdrawal.

Benefit-risk assessment should be revisited when new evidence emerges. Regulators and manufacturers may consider whether the new information changes the product label, target population, recommended dose, monitoring requirements, contraindications or place in therapy. Assessment should also consider whether risk is concentrated in a subgroup, whether risk can be reduced through screening or monitoring, and whether the proposed action could unintentionally reduce access to an important treatment. Decisions are therefore clinical, epidemiological, regulatory and ethical, not simply statistical.

9. Signal management and regulatory action:

Signal management is a structured process that moves from detection to validation, prioritisation, assessment, recommendation, action and follow-up. EMA Good Pharmacovigilance Practices Module IX describes the EU signal-management process, including responsibilities of marketing authorisation holders and regulatory authorities, monitoring of EudraVigilance, signal confirmation, prioritisation and assessment by the Pharmacovigilance Risk Assessment Committee (PRAC) (EMA, 2017). The exact procedures differ between jurisdictions, but the core principles are widely applicable.

Signal validation checks whether the available information supports further evaluation. It includes verification of reports, review of duplicates, assessment of data completeness, examination of known information and consideration of whether the pattern is genuinely new. Prioritisation then considers seriousness, potential public-health impact, exposure, novelty, plausibility, preventability and the urgency of action. A serious emerging risk may require rapid notification and interim measures before a complete epidemiological assessment is available.

Possible regulatory actions range from no change, continued monitoring or a request for additional data to changes in the summary of product characteristics, patient information leaflet, boxed or prominent warnings, contraindications, dose recommendations, laboratory monitoring, restricted distribution, educational materials, risk-management plans or post-authorisation safety studies. In exceptional circumstances, suspension, recall or withdrawal may be necessary. A risk-minimisation measure should address the mechanism of harm and be practical for the people expected to use it.

The effectiveness of a regulatory action should be evaluated after implementation. For example, a label warning may be issued to reduce use in a high-risk group, but follow-up should assess whether prescribers and patients understand the warning, whether prescribing patterns changed, whether the event rate declined and whether unintended consequences occurred. Risk-minimisation plans are not successful merely because an educational document was distributed; they should demonstrate improved knowledge, behaviour or outcomes where measurable.

10. ICH E2D(R1): broader post-approval safety data:

A notable recent development is the final ICH E2D(R1) guideline on post-approval safety data, adopted by the ICH Assembly in September 2025. FDA published its final guidance in March 2026. The revision updates the 2003 E2D framework and clarifies how safety information from newer or increasingly used sources should be handled, including social media, market research programmes, patient-support programmes and other organised data-collection systems (ICH, 2025; FDA, 2026).

The update matters because a patient may describe a suspected reaction during a support call, digital adherence programme, market research interview or online interaction rather than through a conventional spontaneous report. Companies and other responsible organisations need procedures to recognise safety information, determine whether it meets reporting criteria, document source context, follow up where appropriate and submit valid cases in accordance with applicable timelines and regional requirements. The fact that a post appears online does not automatically make it a valid ICSR; the minimum case elements and relevant regulatory definitions still apply.

In the European Union, the revised guideline became applicable on 18 March 2026, with a six-month transition period extending to 18 September 2026. EMA implementation guidance describes the practical treatment of patient-support programmes and organised data collection systems during the transition. As of the review date, organisations operating in the EU should have completed the transition and aligned their procedures with the updated requirements (EMA, 2026). Because local implementation schedules may differ, organisations should verify current requirements with the relevant authority before changing operational processes.

11. Patient-centred pharmacovigilance and risk communication:

Patients are not only recipients of safety information; they are important sources of it. They may report symptoms, changes in daily functioning, treatment burden, adherence problems and effects that are not always fully represented in clinical notes. Direct patient reporting can add the patient's own description of the event and its impact. Van Grootheest and de Jong-van den Berg (2004) described the role of patients in ADR reporting and the rationale for involving them in drug-safety surveillance.

Patient-centred reporting requires accessible routes, clear language, translated forms, mobile and non-digital options, and reassurance that a suspected reaction can be reported without first proving causality. Patients should be advised not to stop or alter prescribed treatment solely because they have submitted a report; they should seek advice from a qualified healthcare professional, especially where abrupt withdrawal may be harmful. Reporting portals should explain how information will be used, how privacy is protected and what follow-up the patient can expect.

Risk communication should be timely, accurate, balanced and actionable. Messages should explain what is known, what remains uncertain, who may be affected, which symptoms require urgent attention and what patients or clinicians should do. Overstating an uncertain signal may create unnecessary fear and discontinuation of beneficial therapy. Understating a serious risk can delay recognition and treatment. Communications should distinguish suspected associations from confirmed causal relationships and should be updated as evidence changes.

Healthcare professionals have a central role in converting safety information into safer practice. Physicians can review treatment necessity, alternatives and patient-specific risks. Pharmacists can identify interactions, duplicate therapy, dose errors, contraindications and adherence problems. Nurses often observe early symptoms, medication administration problems and patient concerns during ongoing care. Multidisciplinary medication review, reconciliation at transitions of care, patient counselling and clear documentation can reduce preventable harm. Safety feedback should return to reporting clinicians and patients so that pharmacovigilance remains a learning system rather than a one-way administrative process.

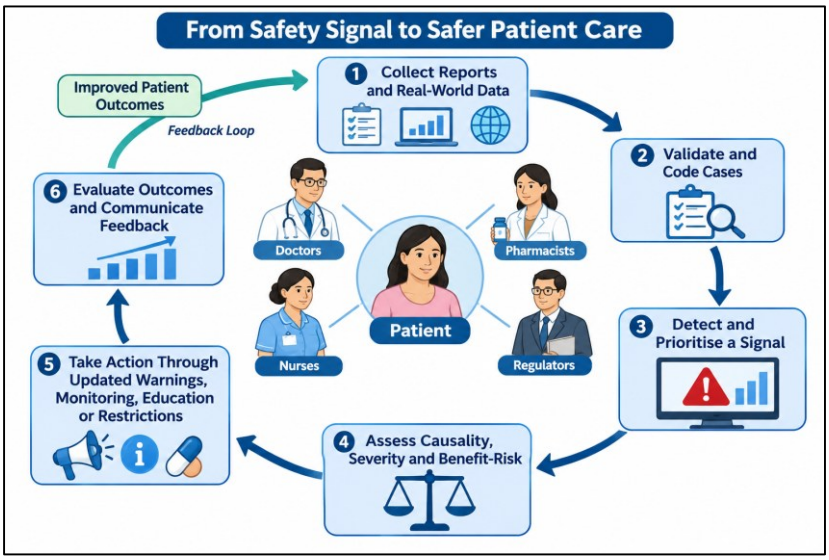


Figure. 2: From Safety Signal to Safer Patient Care: The Six-Stage Pharmacovigilance Cycle for Signal Detection, Risk Assessment, Regulatory Action and Continuous Improvement

12. Challenges and persistent gaps:

Despite technological progress, pharmacovigilance systems continue to face uneven reporting capacity. Countries differ in regulatory resources, workforce training, digital infrastructure, laboratory access and the availability of national safety databases. Under-representation of low- and middle-income countries can reduce the visibility of risks in populations with different genetics, comorbidities, medicine access, environmental exposures and patterns of use. Global databases cannot correct these gaps unless national reporting systems are adequately supported and local context is retained during analysis.

Interoperability remains difficult because healthcare systems use different product identifiers, coding systems, languages, data structures and privacy rules. Standardised terminologies such as MedDRA and internationally aligned ICSR formats improve exchange, but mapping local terms to standard codes may lose clinical nuance. Medicine names can be confused because of brand, generic, combination-product or spelling differences. Robust product dictionaries, coding guidance and regular quality checks are therefore important.

Privacy and cybersecurity must be built into every digital surveillance programme. Health data may contain sensitive personal information, and cross-border data exchange is subject to legal and ethical requirements. Privacy-preserving distributed analysis, de-identification, role-based access, secure transfer, retention controls and transparent governance can reduce risks. De-identification alone does not guarantee anonymity, particularly when several datasets can be linked.

Another challenge is the risk of false alerts and alert fatigue. Large-scale screening can generate thousands of statistical associations, many of which are explained by chance, confounding, data errors or stimulated reporting. Conversely, strict thresholds may miss rare but important harms. Programmes should evaluate the sensitivity and positive predictive value of their detection methods, document decisions not to pursue a signal and periodically reassess the performance of the overall surveillance process. Multiple-testing issues and inconsistent thresholds across studies remain recognised methodological concerns in pharmacovigilance research.

Finally, the effectiveness of pharmacovigilance should be judged by its contribution to safer medicine use, not only by the number of reports received, database searches completed or signals generated. Useful performance measures include report completeness, time from event recognition to reporting, time to signal assessment, timeliness of regulatory action, implementation of risk minimisation, reporting participation across population groups and measurable changes in preventable harm.

13. Future directions:

The next stage of pharmacovigilance is likely to involve the integration of complementary data streams rather than dependence on a single large database. Spontaneous reports will remain valuable for detecting unexpected events, while active surveillance, registries and well-designed observational studies will help quantify and characterise risk. Linking these sources through common data models and interoperable product and event terminology may improve the speed and consistency of safety assessment, provided that governance and privacy protections are robust.

AI and automation are likely to become more useful in targeted tasks such as intake triage, translation support, duplicate identification, structured extraction, case prioritisation and literature screening. High-impact decisions should remain accountable to trained safety professionals. Organisations should publish or document intended use, validation methods, known limitations, human-review steps and post-deployment monitoring. Models should be tested across languages, age groups, clinical settings and product classes to reduce unequal performance.

More patient-generated data may improve recognition of treatment effects that matter to daily life, including fatigue, sleep disruption, cognitive symptoms, and treatment burden and adherence barriers. Digital reporting should not exclude people without smartphones, reliable internet or high health literacy. Hybrid systems that combine digital access with telephone, paper and in-person options are more likely to support inclusive reporting.

The regulatory environment is also moving towards greater methodological harmonisation. ICH E2D (R1) clarifies the management of post-approval safety information from evolving sources, while ICH M14 provides common principles for non-interventional safety studies using RWD. Together, these developments support a more consistent evidence pathway: recognise safety information, validate cases, investigate patterns, conduct fit-for-purpose studies, assess the benefit-risk balance and communicate proportionate action. Global collaboration will be essential because medicines, data and safety concerns do not stop at national borders.

14. Implications for healthcare professionals and institutions:

Hospitals and colleges can strengthen pharmacovigilance by integrating ADR reporting into routine clinical workflows. Every suspected event should prompt a structured review of the patient's medication history, timing of exposure, dose, route, indication, co-medications, relevant investigations and outcome. Institutions should designate trained pharmacovigilance contacts, provide accessible reporting forms, educate staff about the difference between adverse events and ADRs, and give feedback after reports are submitted. Reporting should be encouraged as a learning activity, not treated as an exercise in blame.

Pharmacy and nursing education should include practical skills in recognising suspected reactions, documenting accurate medication histories, identifying interactions, counselling patients, evaluating severity and reporting through national systems. Clinical teams should pay special attention to high-risk medicines, polypharmacy, older adults, paediatric patients, renal or hepatic impairment, pregnancy and transitions between hospital and community care. Medication safety committees can use aggregated local reports to identify preventable patterns and redesign processes such as prescribing, dispensing, preparation, administration and monitoring.

For pharmaceutical companies and research organisations, emerging trends require sound standard operating procedures, trained case processors, validated technology, audit trails and clear oversight of vendors and digital channels. Safety databases should be reconciled and quality-controlled, and periodic reports should integrate clinical, non-clinical, epidemiological and regulatory evidence. The adoption of AI should be governed through documented validation and change control rather than informal use of general-purpose tools for unreviewed safety decisions.

15. Conclusion:

Pharmacovigilance is moving towards an integrated, data-rich and patient-centred model of medicine safety. WHO VigiBase, EudraVigilance, FAERS, FDA Sentinel and national programmes such as India PvPI provide complementary mechanisms for collecting, sharing and analysing safety information. Spontaneous reports remain essential for the early recognition of unexpected harms, while disproportionality methods, active surveillance and real-world studies help prioritise and evaluate potential risks. Statistical signals must be interpreted carefully because reporting databases do not establish incidence or causality. AI and NLP offer practical opportunities to improve efficiency, but reliable implementation requires external validation, transparency, privacy protection and human oversight. Recent ICH E2D (R1) and M14 guidance reinforce the need for harmonised standards across evolving data sources and real-world safety studies. Ultimately, the value of pharmacovigilance lies in converting reliable evidence into timely, proportionate action that protects patients while preserving access to medicines whose benefits outweigh their risks.

16. References:

(1) World Health Organization. The WHO Programme for International Drug Monitoring [Internet]. Geneva: World Health Organization; [cited 2026 Oct 31]. Available from: https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance/networks/pidm
(2) Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. Lancet. 2000;356(9237):1255-9. doi:10.1016/S0140-6736(00)02799-9.
(3) US Food and Drug Administration. M14: general principles on planning, designing, analysing, and reporting of non-interventional studies that utilise real-world data for safety assessment of medicines [Internet]. Silver Spring (MD): FDA; 2026 Mar [cited 2026 Oct 31]. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/m14-general-principles-planning-designing-analyzing-and-reporting-non-interventional-studies-utilize.
(4) European Medicines Agency. EU implementation strategy of ICH E2D(R1) guideline: post-approval safety data, definitions and standards for management and reporting of individual case safety reports [Internet]. Amsterdam: EMA; 2026 [cited 2026 Oct 31]. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/eu-implementation-strategy-ich-e2dr1-guideline-post-approval-safety-data-definitions-standards-management-reporting-individual-case-safety-reports_en.pdf.
(5) Hazell L, Shakir SAW. Under-reporting of adverse drug reactions: a systematic review. Drug Saf. 2006;29(5):385-96. doi:10.2165/00002018-200629050-00003.
(6) Council for International Organizations of Medical Sciences. Practical aspects of signal detection in pharmacovigilance: report of CIOMS Working Group VIII. Geneva: CIOMS; 2010.
(7) Bate A, Evans SJW. Quantitative signal detection using spontaneous ADR reporting. Pharmacoepidemiol Drug Saf. 2009;18(6):427-36. doi:10.1002/pds.1742.
(8) Harpaz R, DuMouchel W, Shah NH, Madigan D, Ryan P, Friedman C. Novel data-mining methodologies for adverse drug event discovery and analysis. Clin Pharmacol Ther. 2012;91(6):1010-21. doi:10.1038/clpt.2012.50.
(9) European Medicines Agency. Guideline on good pharmacovigilance practices (GVP): Module IX - Signal management (Rev 1) [Internet]. Amsterdam: EMA; 2017 [cited 2026 Oct 31]. Available from: https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/pharmacovigilance-post-authorisation/good-pharmacovigilance-practices-gvp
(10) European Medicines Agency. EudraVigilance system overview [Internet]. Amsterdam: EMA; [cited 2026 Oct 31]. Available from: https://www.ema.europa.eu/en/human-regulatory-overview/research-development/pharmacovigilance-research-development/eudravigilance/eudravigilance-system-overview
(11) US Food and Drug Administration. FDA Adverse Event Reporting System (FAERS) [Internet]. Silver Spring (MD): FDA; [cited 2026 Oct 31]. Available from: https://open.fda.gov/data/faers/

(12) US Food and Drug Administration, Office of Surveillance and Epidemiology. 2025 annual report: Office of Surveillance and Epidemiology [Internet]. Silver Spring (MD): FDA; 2026 [cited 2026 Oct 31]. Available from: https://www.fda.gov/media/195212/download
(13) Indian Pharmacopoeia Commission. Pharmacovigilance Programme of India: profile [Internet]. Ghaziabad: IPC; 2025 [cited 2026 Oct 31]. Available from: https://www.ipc.gov.in/images/PvPI_Profile_-_19.9.2025.pdf
(14) van Grootheest K, de Jong-van den Berg L. Patients' role in reporting adverse drug reactions. Expert Opin Drug Saf. 2004;3(4):363-8. doi:10.1517/14740338.3.4.363.
(15) US Food and Drug Administration. E2D(R1) post-approval safety data: definitions and standards for management and reporting of individual case safety reports [Internet]. Silver Spring (MD): FDA; 2026 Mar [cited 2026 Oct 31]. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e2dr1-post-approval-safety-data-definitions-and-standards-management-and-reporting-individual-case
(16) International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. ICH M14: general principles on planning, designing, analysing, and reporting of non-interventional studies that utilise real-world data for safety assessment of medicines [Internet]. Geneva: ICH; 2025 [cited 2026 Oct 31]. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/ich-m14-guideline-general-principles-planning-designing-analysing-reporting-non-interventional-studies-utilise-real-world-data-safety-assessment-medicines-step-5_en.pdf
(17) Li Y, Tao W, Li Z, Sun Z, Li F, Fenton S, et al. Artificial intelligence-powered pharmacovigilance: a review of machine and deep learning in clinical text-based adverse drug event detection for benchmark datasets. J Biomed Inform. 2024;152:104621. doi:10.1016/j.jbi.2024.104621.
(18) Warner J, Prada Jardim A, Albera C. Artificial intelligence: applications in pharmacovigilance signal management. Pharm Med. 2025;39(3):183-98. doi:10.1007/s40290-025-00561-2.
(19) Taherifard E, Ross JS, Ramachandran R, Wallach JD. US Food and Drug Administration Sentinel Initiative and postmarket drug safety surveillance: a review. JAMA Health Forum. 2026;7(4):e260754. doi:10.1001/jamahealthforum.2026.0754.
(20) El Sayed I, Bedwany RN, Salama M, Eltrass ASH. Integration of artificial intelligence into pharmacovigilance: a systematic review. Res Social Adm Pharm. 2026 Sep 30. doi:10.1016/j.sapharm.2026.09.001.