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# Pharmacovigilance and Marketing Authorizations Holders of Pharma pdts

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**Abstract:** In modern healthcare, pharmacovigilance (PV) offers critical advantages that impact pharmaceutical products throughout their life cycle. Modern health care benefits significantly from the practice of pharmacovigilance, which monitors drug safety and efficacy throughout the product life-cycle (1). Although a pharmaceutical product is rigorously tested prior to approval, unforeseen side effects may arise after authorization due to insufficient sample size, length, and heterogeneity of studied populations (2). This phenomenon is responsible for long-term and rare side effects of drugs being identified only after they have been widely prescribed (3). As such, post-marketing surveillance is critical for protecting public health (4). The decision of a regulatory authority to authorize a medicine is a marketing authorization that rests on an assessment that the proposed drug's advantages outweigh its risks for a particular indication and in a particular patient group (5). The U.S. Food and Drug dministration (FDA), the European Medicines Agency (EMA), and the Central Drugs Standard ontrol Organization (CDSCO) in India mandate that Marketing Authorisation Holders (MAHs) maintain vigilance for adverse effects of approved drugs, report novel safety issues, implement appropriate pharmacovigilance mechanisms, and update relevant product literature with information on new risks (6,7). Risk Management Plans (RMPs) and Periodic Safety Update Reports (PSURs) are required, ensuring a continuous risk–benefit evaluation throughout the product life cycle (8,9). Modern pharmacovigilance systems collect data from multiple sources including spontaneous reports of adverse drug reactions (ADRs), electronic health records, registries, health insurance claims data, real-world evidence, and direct patient reports, which contribute to increased quantity and diversity of safety information (10). However, an overwhelming number of ADRs are reported globally, necessitating enhanced reporting mechanisms and training (11). Technologies such as artificial intelligence, machine learning, and Big Data Analytics have revolutionized the pharmacovigilance system by enhancing signal detection and risk evaluation (12). Several challenges including inadequate reporting rates, quality of information, diverse regulatory systems globally, and insufficient infrastructure in developing countries have hampered the efficacy of pharmacovigilance systems. The system has evolved beyond mere reporting to a holistic life-cycle concept to track medicines safety, enabling continuous evaluation of the benefit–risk profile and protection of patients against harm (14). Close partnership of regulators, healthcare providers, pharmaceutical companies, and patients remains key to sustaining public confidence in medicines and raising global healthcare safety standards (15).

**Keywords:** Pharmacovigilance; Marketing Authorisation; Drug Safety; Adverse Drug Reactions; Post-Marketing Surveillance; Benefit–Risk Assessment; Regulatory Affairs; Signal Detection; Risk Management Plan (RMP); Periodic Safety Update Report; Pharmacovigilance System Master File; Marketing Authorisation Holder; Real-World Evidence; Patient Safety; Drug Regulation.

## 1. INTRODUCTION

Pharmacovigilance developed in reaction to major medication-safety disasters during the middle of the twentieth century (1) . Its main purpose is to confirm, from early laboratory work through post-market monitoring, that therapeutic benefits remain greater than associated harms (2). Today, the field covers more than standard drugs, extending to biologics, advanced treatments including gene and cell-based therapies, plant-based remedies, and animal-health products (3). The World Health Organization (WHO) describes pharmacovigilance as 'the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems' (4). Across time, pharmacovigilance has moved beyond passive reporting alone to also incorporate real-world evidence (RWE), artificial intelligence (AI), monitoring of online content, and outcomes reported by patients (5).

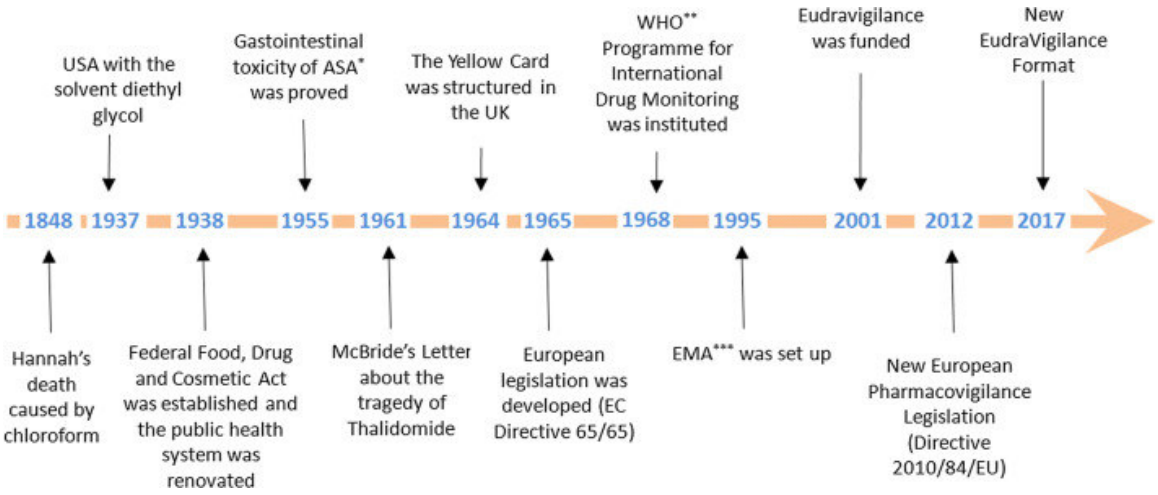

**Figure 1.** Overview of the pharmacovigilance lifecycle including data collection, signal detection, regulatory reporting, and risk management activities.

## 2. Historical Evolution of Pharmacovigilance

### 2.1 Early Beginnings

Pharmacovigilance originated from one of the first recorded drug-related tragedies to occur in medical history. A 1848 incident involving Hannah Greener, a young girl from Northern England who died under chloroform anesthesia , was significant in that it placed fears into the heart of physicians about the dangers related to anesthetics . Even though a thorough investigation into the incident did not definitively determine what caused Hannah's death to have occurred, there continues to be speculation among modern-day medical professionals that her death was caused by heart arrhythmia or aspiration into the lungs from the chloroform used during the procedure. This case also stands as an early indication that we must take great care to monitor both drug safety and drug-related adverse reactions even after the approval and use of a drug within a clinical setting within the time frame of its use. By the 1960s when the tragedy of thalidomide became widely known, the importance of pharmacovigilance was further driven home. Thalidomide had been prescribed to many pregnant women for nausea and to help with difficulties getting to sleep; however, later it was discovered that it created major complications including severe birth defects related to bone deformities in babies born to women who took thalidomide during their pregnancies. Subsequently, several countries developed national pharmacovigilance centers , and in 1968 the World Health Organization (WHO) initiated the Programme for International Drug Monitoring to facilitate global collaboration in drug safety surveillance. Since then, pharmacovigilance has expanded into a

comprehensive scientific discipline that plays a central role in public health by ensuring the ongoing evaluation of the benefit-risk profile of medicines throughout their lifecycle (7).




## 2.2 Regulatory Milestones

Key regulatory developments shaped modern pharmacovigilance: In 1962, the Kefauver–Harris Amendments in the United States required assessment and reporting of adverse events for medicines (8). The World Health Organization established the Programme for International Drug Monitoring, building an international network to exchange safety information (9). Nations including the UK (Yellow Card Scheme) and Canada (Canada Vigilance Program) established strong systems for monitoring safety after marketing (10). These foundational initiatives established the regulatory infrastructure upon which contemporary pharmacovigilance systems are built.

## 2.3 Modern Expansion

As global markets and technology progressed, pharmacovigilance expanded to cover digital health solutions, analysis of massive datasets, artificial intelligence-based signal identification, and aligned cross-border standards (11,12). Contemporary systems now integrate sophisticated computational methods with traditional reporting mechanisms, representing a fundamental shift in how medicines safety is monitored and evaluated globally.

## 3. Core Components of Pharmacovigilance Systems

Pharmacovigilance systems aim to find, assess, and reduce risks linked to medicines across the product's lifespan (13). They depend on multiple interconnected functions. Adverse drug reaction monitoring continues to be pharmacovigilance's central element (14). Clinicians, manufacturers, and the public feed spontaneous reporting channels that enable early recognition of new safety concerns (15). Risk Management Plans (RMPs) provide organized approaches for spotting possible safety issues and applying measures to limit risk (16). Regulators frequently expect Risk Management Plan submission as part of an application for marketing authorization (17). Post-marketing surveillance systems include spontaneous reporting systems, observational studies, patient registries, real-world evidence collection, active surveillance systems, and Periodic Safety Update Reports (PSURs) (18). Increasingly, contemporary pharmacovigilance uses digital tools such as electronic health records, data-mining platforms, and predictive methods to enhance the effectiveness of signal detection (19).

## 4. Core Activities in Pharmacovigilance

### 4.1 Pre-Marketing Safety Assessment

Prior to authorization, medicines complete demanding preclinical work (including novel approach methods that use human-derived in vitro materials) and staged clinical trials intended to reveal possible risks (20). However, these investigations typically include small groups and can miss uncommon or delayed harmful outcomes (21). This limitation necessitates the implementation of rigorous post-marketing surveillance to identify safety signals that emerge in larger, more diverse populations (22).

### 4.2 Post-Marketing Surveillance

After release, medicines are monitored using multiple complementary approaches. Spontaneous reporting systems enable clinicians and patients to submit suspected adverse drug reactions (ADRs) (23). Active surveillance encompasses cohort-based research drawing on electronic health records (EHRs), registries, claims databases, mobile apps, wearable devices, and social-media monitoring (25). Signal detection using quantitative techniques, including disproportionality analyses, supports discovery of unanticipated safety patterns within large data collections (26).

### 4.3 Signal Management and Risk Minimization

Signal management covers spotting possible safety problems ('signals'), judging their credibility and significance, sharing conclusions with relevant parties, and putting risk-reduction actions in place, such as label updates or limiting use (27). This systematic approach ensures that emerging safety concerns are rapidly identified and appropriately communicated to healthcare providers and patients.

## 5. Global Regulatory Frameworks and Harmonization

### 5.1 International Guidelines and Organizations

Major organizations that influence worldwide pharmacovigilance include the World Health Organization (WHO), the International Council for Harmonisation (ICH), the European Medicines Agency (EMA), and the U.S. Food and Drug Administration (FDA) (28,29). Together, these organizations have established expectations that include Periodic Safety Update Reports (PSURs), Risk Management Plans (RMPs), ICH E2E guidance for pharmacovigilance planning, and systems for near-real-time signal identification (30,31). This collaborative approach has substantially improved the consistency and effectiveness of pharmacovigilance practices across regulatory jurisdictions.

### 5.2 Regional Approaches and Challenges

Even as harmonization efforts continue, regional variations persist . In the United States, FDA guidance places strong emphasis on post-market obligations, requiring comprehensive reporting and analysis (33). The European Union has integrated pharmacovigilance throughout the full product lifecycle with forward-looking risk control mechanisms (34). In countries such as India, pharmacovigilance capacity is expanding rapidly, though scale and limited resources create distinct challenges (35). In lower- and middle-income settings, scarce resources and training contribute to low reporting levels, yet regional partnerships are helping drive improvement (36).

### 5.3 Special Populations and Advanced Products

Pharmacovigilance systems are being reshaped to suit advanced therapy medicinal products (ATMPs), plant-based or traditional remedies ('phytovigilance'), animal medicines ('veterinary pharmacovigilance'), and individualized care models that incorporate pharmacogenetics and

genomics (7,8). These specialized applications reflect the expanding complexity and diversity of modern pharmaceutical products.

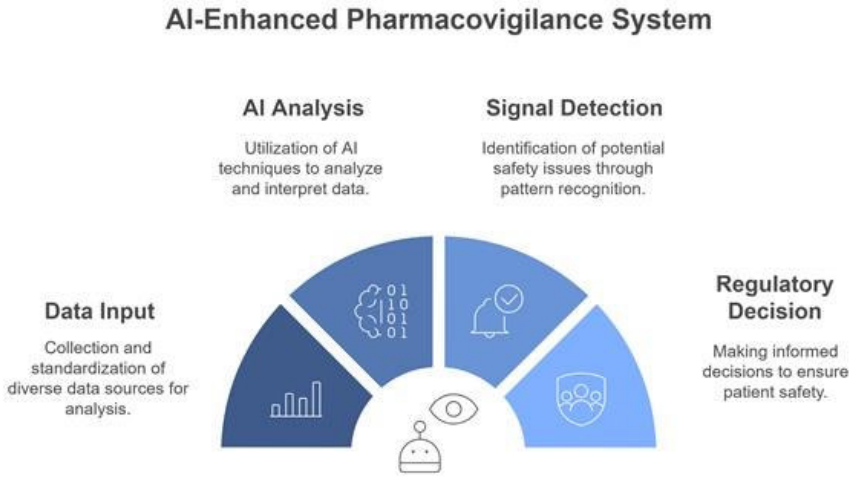
## 6. Methodological Innovations in Pharmacovigilance

### 6.1 Real-World Evidence and Digital Tools

Information drawn from electronic health records, insurance claims sources, and mobile health applications or wearables adds perspectives that controlled clinical trials cannot capture, supporting faster recognition of adverse drug reactions across varied populations (3). Monitoring online platforms is becoming an additional route for post-approval oversight; however, this approach must be assessed carefully because of potential noise and bias in unstructured data (4).

### 6.2 Artificial Intelligence and Digital Pharmacovigilance

Emerging technologies have enabled transformation of pharmacovigilance across the globe (4). In particular, artificial intelligence combined with data science has allowed healthcare datasets to be reviewed to identify safety signals beyond the constraints of traditional manual reviews (3). Specific technological applications include computational linguistics for natural language processing of unstructured safety reports, integration of electronic health records for signal detection, predictive analytics for identifying emerging risks, Big Data analysis for pattern recognition, and social media monitoring for real-time pharmacovigilance signals (4,5). Each of these tools has the potential to detect safety issues with medications in a more timely manner (6). However, these tools have important limitations and cannot fully identify safety signals due to concerns such as lack of control over the data being analyzed, lack of transparency in algorithmic reasoning, and uneven distribution of data used in the analysis (7).




### 6.3 Advanced Statistical Methods

Current pharmacovigilance employs Bayesian and frequentist techniques to enable adaptive safety tracking, improving the detection of emerging risks (8). Ensemble clustering approaches enhance detection of unusual patterns in post-approval datasets (9). Federated analysis supports collaboration across multiple sites without exchanging raw patient-level records, helping protect privacy while strengthening the reliability of detected signals (5).

## 7. Real-World Evidence in Post-Marketing Safety

Observational studies drawing on claims databases, electronic health records, registries, and spontaneous-reporting systems are now indispensable for extending trial evidence . However,

these studies remain vulnerable to serious methodological weaknesses and data limitations. Bias can arise from the data source itself, from incomplete records, or from weak study design . For this reason, it is necessary to judge whether a dataset is truly 'fit for purpose,' and this assessment must be backed by strict methodological standards (6).

### 7.1 Case Examples of Real-World Evidence in Practice

Researchers analyzing the FDA Adverse Event Reporting System (FAERS) identified the post-approval safety profile of Enfortumab vedotin and detected strong signals for severe skin reactions and peripheral neuropathy, along with numerous preferred terms not appearing in the product labeling .Analysis of Vaccine Adverse Event Reporting System (VAERS) reports for RSV vaccines identified disproportionate reporting of important medical events, including signals related to pregnancy, and mapped onset timing in a way that is useful for clinical vigilance .Privacy-preserving linkage of real-world datasets has been proposed as a method for long-term safety follow-up . This approach may help uncover rare harms and delayed adverse effects while feeding real-world signals into risk-management plans without crossing privacy regulations such as HIPAA or ethical boundaries (8).

## 8. Marketing Authorization and the Role of Marketing Authorisation Holders

The core aim of pharmacovigilance is to keep medicines safe and effective across the full span of their use . Work on this begins far earlier than a product's first sale . Across the globe, regulatory authorities including the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) require demanding laboratory and clinical assessments to verify quality, safety, and therapeutic benefit . However, because trials can be brief, include few participants, and exclude certain population groups, some hazards will not be discovered before a license is granted . For this reason, monitoring after launch is essential, and the legal responsibility for this ongoing surveillance falls primarily on the marketing authorization holder (6).

### 8.1 Safety Requirements Before Marketing Authorization

For a marketing authorization to be obtained, applicants must provide extensive evidence covering quality, effectiveness, and safety (4). In certain geographic areas, including Tanzania, regulations for herbal products permit regulators to rely largely on long-standing traditional use and the published record because applications often lack the necessary preclinical and clinical safety evidence (5). Within the European Union, a Risk Management Plan (RMP) must be included in the initial marketing authorization submission and with any substantial subsequent changes (16). The RMP lays out known and possible risks, together with commitments to run post-authorization safety studies . Skilled medical writing is crucial at this stage to correctly produce the core safety documents that guide marketing authorization outcomes (8).

### 8.2 Ongoing Duties of Marketing Authorization Holders

By law, marketing authorization holders must keep ongoing surveillance of the safety profile of their products, inform regulators about any changes that could affect the marketing authorization, and keep prescribing information up to date (9). They are required to record every suspected adverse drug reaction whether it comes from unsolicited reports or post-authorization research and to maintain a strong quality framework along with a Pharmacovigilance System Master File (PSMF) (7). Regulatory environments in places such as India and Tanzania reflect similar requirements, obligating marketing authorization holders to gather adverse drug reactions, provide Periodic Safety Update Reports, name a qualified pharmacovigilance lead, and maintain internal quality arrangements . However, adherence is uneven, especially among herbal manufacturers . In China, newer regulatory changes require

marketing authorization holders to report adverse drug reactions themselves and to file yearly pharmacovigilance overviews in line with detailed national instructions .

In addition, marketing authorization holders must actively review external safety resources such as WHO Vigi Base , Eudra Vigilance, and FAERS together with the scientific literature, to spot new risks that could require label revisions or modifications to the marketing authorization (6).

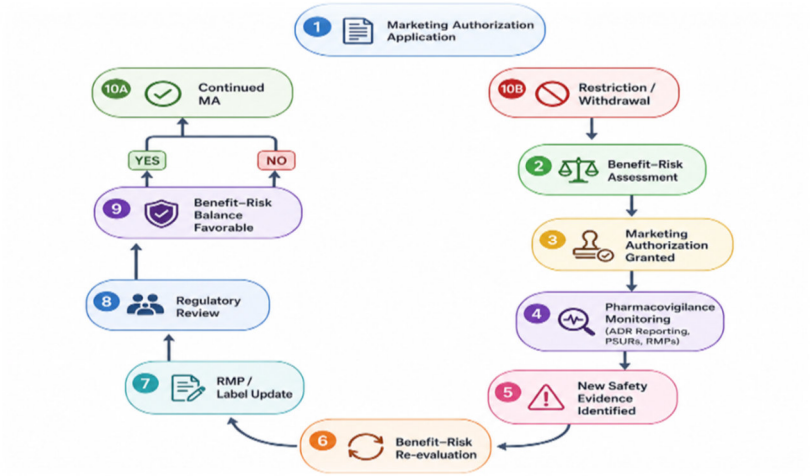
### 8.3 Post-Authorization Activities and Lifecycle Oversight

After approval, products undergo intensive post-market monitoring . Marketing authorization holders need to manage adverse drug reaction case handling, perform signal identification, and repeatedly re-evaluate the benefit–risk relationship (7). The introduction of COVID-19 vaccines showcased how demanding this becomes, as marketing authorization holders had to handle extraordinary quantities of safety reports and publications to preserve their authorizations . National authorities issue and renew marketing authorizations and run adverse drug reaction reporting systems while also carrying out inspections . However, these agencies' effectiveness can be reduced when spontaneous reporting is low (8). Audits in areas such as Europe and Saudi Arabia often find marketing authorization holder shortfalls involving Pharmacovigilance System Master Files, the placement of qualified pharmacovigilance staff, and adverse drug reaction operations indicating that strong pharmacovigilance is not just paperwork, but a firm requirement for keeping marketing authorization status (8).To boost efficiency while meeting regulatory expectations, current approaches include risk-based follow-up for Individual Case Safety Reports (ICSRs) and tighter monitoring of Risk Management Plan obligations (5).

## 9. Benefit–Risk Evaluation and Lifecycle Management

Keeping the benefit–risk balance favorable is required for continued marketing authorization, which demands organized reviews that use pharmacovigilance evidence throughout the product's full lifespan (6). Maintaining approval is not unconditional; it depends on the marketing authorization holder continuing to watch for safety issues, notifying authorities about new threats, and revising labeling when needed (7).

In the European Union, Risk Management Plans function as living documents that must be revised whenever fresh evidence changes the benefit–risk balance or when key post-authorization studies finish (8). A comprehensive review of 64 European Union Risk Management Plans spanning seven products over 14 years demonstrated that as regulatory guidance evolved, safety topics became fewer yet more specific (9). Furthermore, the steady accumulation of clinical, non-clinical, and post-market evidence enabled regulators to reclassify or remove more than 40 previously identified risks or gaps in knowledge (19). This dynamic approach ensures that benefit–risk assessments remain current and evidence-based throughout a product's commercial life.




## 10. Pharmacovigilance for Advanced Therapy Medicinal Products

Advanced therapy medicinal products (ATMPs), including gene therapies and cell-based treatments, create unique challenges in pharmacovigilance due to their complex structure and the potential for delayed adverse effects . Safety assessment is complicated by immunogenicity and batch-to-batch variation, and is further challenged by the requirement for long-term monitoring that does not exist in traditional medicines . Gene therapies and cell-based treatments require more intensive long-term monitoring due to the potential of adverse effects emerging many years after the treatment has been administered .In most of the world's leading regions, each approved advanced therapy medicinal product is subject to mandatory post-authorization requirements to monitor the long-term safety and efficacy . This regulatory approach reflects concerns regarding very late adverse events that may result from the potential irreversible nature of single-administration gene or cell-based therapeutic products (27).

## 11. Challenges Facing Pharmacovigilance Systems

### 11.1 Underreporting and Data Quality Issues

Globally, failure to report remains one of the biggest weaknesses particularly in resource-limited settings because clinicians or patients may lack awareness or training . Uneven vocabularies and mismatched data fields also make pooling and comparing data across platforms more difficult (10). Some estimates suggest that recorded adverse drug reactions represent less than one in ten of all cases, highlighting the critical need for improved reporting mechanisms and training .

### 11.2 Integration Across Lifecycle and Stakeholders

Smooth alignment between manufacturing quality assurance and pharmacovigilance workflows is critical even long-established generics may acquire fresh hazards if production or distribution failures occur (12). Working jointly across regulators, companies, researchers, and patients is essential to communicate risks effectively and ensure comprehensive safety oversight (13).

### 11.3 Ethical and Privacy Considerations

When precision pharmacovigilance uses genetic and personalized information, it creates ethical challenges involving informed consent and protection of data . Equitable access is necessary so that all communities benefit from improved drug-safety oversight (16).

## 12. Future Directions: Toward Proactive and Predictive Pharmacovigilance

Pharmacovigilance is evolving toward more sophisticated, anticipatory, and globally coordinated approaches. Looking ahead, pharmacovigilance frameworks will likely shift further toward patient focus, stronger reliance on technology, and tighter international alignment, while regulatory science continues to be reshaped to address issues linked to biologic products, individualized therapies, and digital health tools (20).Key directions developing now include: Pharmacovigilance aided by artificial intelligence to enhance signal detection capabilities; Safety infrastructures supported by blockchain technology for improved data integrity and traceability; Worldwide safety repositories updated in real time to enable rapid knowledge dissemination; Greater involvement and empowerment of patients in safety reporting and assessment; More sophisticated methods for predictive signal finding using machine learning algorithms; Integration of genomic information within safety surveillance to support personalized medicine approaches; Enhanced coordination between regulators, healthcare providers, pharmaceutical manufacturers, and patient advocacy organizations (21). International alignment initiatives, driven by bodies like the WHO, ICH, EMA, and FDA, continue to strengthen uniformity in how countries oversee medicine safety (11).

It is increasingly common to see pharmacovigilance that is patient-focused and values the lived experience of patients. Patients routinely report their own negative outcomes to regulators, which helps regulatory authorities understand the safety concerns of products that they encounter in clinical practice. This patient-centered perspective represents a fundamental shift toward more comprehensive and holistic approaches to medicine safety (14).

## 13. Lessons from Notable Cases: Importance of Post-Marketing Surveillance

### 13.1 Thalidomide

In the 1960s, thalidomide led to profound birth defects in many thousands of newborns and fundamentally reshaped medicine oversight worldwide. This catastrophe demonstrated the critical importance of post-marketing surveillance and the need for regulatory systems capable of rapidly identifying and responding to unexpected adverse effects (6,11).

### 13.2 Rofecoxib (Vioxx)

The Rofecoxib (Vioxx) case represents one of the most noteworthy examples of recent pharmacovigilance. Although Rofecoxib was approved as a pain and arthritis medication, subsequent studies revealed a long-term association with increased cardiovascular risk (28). The medicine was withdrawn from the market once post-authorization safety studies demonstrated the magnitude of this risk. This case illustrated the critical need for ongoing post-marketing vigilance to evaluate the safety of medicines throughout their availability to the public and the importance of comprehensive communication of safety concerns (20). It underscores how continued benefit–risk assessment throughout a product's life cycle is essential for protecting patient safety (21).

## 14. The Pharmacovigilance Program of India

With the establishment of the Pharmacovigilance Program of India (PvPI), India has greatly enhanced its national pharmacovigilance infrastructure. Established under the Indian Pharmacopoeia Commission, this program facilitates the monitoring of medicine safety across hospitals, medical colleges, and healthcare institutions throughout the country (23).The key activities undertaken by the Pharmacovigilance Program of India include: collection and evaluation of reports on adverse drug reactions; identification of safety signals and evaluation of risks; training of healthcare professionals in pharmacovigilance; raising awareness in the general public about medication safety; and surveillance of vaccines and medical devices (24).

The presence of more than 150 Adverse Drug Reaction Monitoring Centers in India demonstrates the increase in participation toward the reporting of medicine safety and reflects the program's success in building national pharmacovigilance capacity (25).

### 15. Ethical and Patient-Centric Dimensions of Pharmacovigilance

Pharmacovigilance naturally connects with ethical practices in healthcare (26). Each safety report concerns a real patient whose wellbeing depends on accurate safety monitoring (27). The success of such a system is founded on regulators, healthcare personnel, and pharmaceutical representatives maintaining a firm belief in the system of safety assessments and sustaining the trust of patients (28).The increase in reported adverse effects by patients results from the shift toward patient-centered healthcare approaches and the movement toward shared responsibility in medicine safety (29). Empowering patients to participate actively in pharmacovigilance represents both an ethical imperative and a practical strategy for improving safety outcomes (30). As pharmacovigilance systems mature, recognition of patient autonomy, informed consent, and the right to accurate safety information becomes increasingly central to the field's evolution (31).

### 16. Conclusion

Pharmacovigilance is now a cornerstone of the modern healthcare ecosystem, offering essential protection to the public by continuously re-assessing the safety of therapeutic agents (32). Despite significant advances in harmonized regulations and the integration of sophisticated technology, numerous challenges persist particularly underreporting, multi-stakeholder coordination difficulties, ethical and data privacy concerns, and inequities between regions, products, and populations (3,13). To maintain public trust while keeping pace with rapid advancements in science and medicine, pharmacovigilance requires a forward-looking approach that combines efficient regulatory frameworks, advanced analytics, and genuine engagement of all stakeholders (34,35).

Contemporary pharmacovigilance systems integrate traditional spontaneous reporting with formal global guidance, real-world evidence, patient engagement, and innovative tools such as artificial intelligence (36). The evidence demonstrates that safety oversight is moving toward more proactive and comprehensive data collection and progressive global harmonization, while facing persistent challenges including underreporting, cognitive biases, and inconsistent regulatory environments across jurisdictions (37). Moving forward, the pharmacovigilance community must prioritize enhanced communication among all stakeholders, development of more robust infrastructure in resource-limited settings, and continued evolution of methodological approaches to ensure that medicines remain safe and effective throughout their entire lifecycle (38). Marketing authorization holders play a central role in this evolving landscape, bearing legal and ethical responsibilities that extend from the pre-approval period throughout the product's commercial life. Their commitment to rigorous pharmacovigilance, transparent communication of risks, and integration of emerging evidence into risk management strategies is fundamental to sustaining both regulatory confidence and public trust in the safety of medicines. Only through coordinated action by regulators, manufacturers, healthcare providers, and patients can we fully realize the promise of pharmacovigilance to protect and advance global public health (39).

## REFERENCES

1. Beninger P. Pharmacovigilance: An Overview. *Clin Ther*. 2018;40(12):1991-2004. doi:10.1016/j.clinthera.2018.07.012
2. Mammì M, Citraro R, Torcasio G, Cusato G, Palleria C, Di Paola E. Pharmacovigilance in pharmaceutical companies: An overview. J Pharmacol Pharmacother. 2013;4:S33-S37.

3. Lucas, S., Ailani, J., Smith, T. R., Abdrabboh, A., Xue, F., & Navetta, M. S. (2022). Pharmacovigilance: reporting requirements throughout a product's lifecycle. Therapeutic advances in drug safety, 13, 20420986221125006. https://doi.org/10.1177/20420986221125006
4. Talbot J, Nilsson B. Pharmacovigilance in the pharmaceutical industry. Br J Clin Pharmacology. 1998;45(5):427-431.
5. Alomar M, Tawfiq A, Hassan N, Palaian S. Post marketing surveillance of suspected adverse drug reactions through spontaneous reporting: current status, challenges and the future. Ther Adv Drug Saf. 2020;11:2042098620938595.
6. Tarkasband A. Review on pharmacovigilance. Int J Res Appl Sci Eng Technol. 2025;13(1):2348-2350.
7. Lavertu, A., Vora, B., Giacomini, K. M., Altman, R., & Rensi, S. (2021). A New Era in Pharmacovigilance: Toward Real-World Data and Digital Monitoring. Clinical pharmacology and therapeutics, 109(5), 1197–1202. https://doi.org/10.1002/cpt.2172
8. Basile A, Yahi A, Tatonetti N. Artificial intelligence for drug toxicity and safety. Trends Pharmacology Sci. 2019;40(12):903-925.
9. Fornasier G, Francescon S, Leone R, Baldo P. An historical overview over pharmacovigilance. Int J Clin Pharm. 2018;40:744-747.
10. Mansuri A, Zaman T. Pharmacovigilance: a necessary tool for drug safety monitoring globally. J Drug Deliv Ther. 2024;14(4):1-8.
11. Raj, N., Fernandes, S., Charyulu, N. R., Dubey, A., G S, R., & Hebbar, S. (2019). Postmarket surveillance: a review on key aspects and measures on the effective functioning in the context of the United Kingdom and Canada. *Therapeutic advances in drug safety*, *10*, 2042098619865413. https://doi.org/10.1177/2042098619865413
12. Beilmann M, Adkins K, Boonen H, Hewitt P, Hu W, Mader R, et al. Application of new approach methodologies for nonclinical safety assessment of drug candidates. Nat Rev Drug Discov. 2025;24:705-725.
13. Chuang-Stein C, Xia H. The practice of pre-marketing safety assessment in drug development. J Biopharm Stat. 2013;23:25-43.
14. Wasiullah W, Yadav Y, Maury S, Vishwakarma M, Yadav A. From clinical trials to post-marketing surveillance: the evaluation of safety data generation in pharmacovigilance. Int J Pharm Res Appl. 2025;14:2595-2601.
15. Beninger P. Signal management in pharmacovigilance: a review of activities and case studies. Clin Ther. 2020;42(3):382-397.
16. Dang A. Real-World Evidence: A Primer. Pharmaceut Med. 2023;37(1):25-36. doi:10.1007/s40290-022-00456-6
17. Hammad T, Naylor M, Ely D, Davies S. Exploring the complexities of disproportionality analysis in pharmacovigilance: reflections on the READUS-PV guideline and a call to action. Front Pharmacology. 2025;16:1573353.
18. Ding Y, Markatou M, Ball R. An evaluation of statistical approaches to postmarketing surveillance. Stat Med. 2020;39:845-874.
19. Chakraborty S, Tiwari R. A clustering ensemble method for drug safety signal detection in post-marketing surveillance. Ther Innov Regul Sci. 2024;59:89-101.
20. Santoro A, Genov G, Spooner A, Raine J, Arlett P. Promoting and protecting public health: how the European Union pharmacovigilance system works. Drug Saf. 2017;40:855-869.

21. Gomes K, Da Silva R, Da Silva J, Bosio C, Novaes M. Post-marketing authorisation safety and efficacy surveillance of advanced therapy medicinal products in Brazil, the European Union, the United States and Japan. Cytotherapy. 2023;25:894-902.

22. Salcher-Konrad M, Naci H, Davis C. Approval of cancer drugs with uncertain therapeutic value: a comparison of regulatory decisions in Europe and the United States. Milbank Q. 2020;98:1219-1256.

23. Lau F, Seifert R. Comparison of drug approvals of the FDA and EMA between 2013 and 2023. Naunyn Schmiedebergs Arch Pharmacol. 2025;399:279-299.

24. Argotti U, Leyens L, Lisbona C, López P, Alonso-Orgaz S, Nevado A, et al. Comparison of the Latin America regulation landscape and international reference health authorities to hasten drug registration and clinical research applications. Ther Innov Regul Sci. 2023;57:1287-1297.

25. Xie J, Li J, Liu Y, Wang H, Wang Y, Yang Y, et al. Comparison of novel oncology drugs that received dual approval from the US accelerated approval and EU conditional marketing authorisation pathways, 2006–2021: a cross-sectional study. BMJ Open. 2023;13:e069132.

26. Tsintis P, Mache EL. CIOMS and ICH initiatives in pharmacovigilance and risk management: overview and implications. Drug Saf. 2004;27(8):509-517.

27. Blackburn S, Arlett P. Benefit risk management plans. Pharm Med. 2013;27(1):5-8.

28. Tubach F, Lamarque-Garnier V, Castot A. Role of the post-marketing authorisation studies in drug risk surveillance: specifications and methodologies. Therapie. 2011;66(4):355-362.

29. Ahonkhai V, Martins SF, Portet A, Lumpkin M, Hartman D. Speeding access to vaccines and medicines in low- and middle-income countries: a case for change and a framework for optimized product market authorization. PLS ONE. 2016;11(11):e0166515.

30. Borg JJ, Aislaitner G, Pirozynski M, Mifsud S. Strengthening and rationalizing pharmacovigilance in the EU: where is Europe heading to. A review of the new EU legislation on pharmacovigilance. Drug Safety . 2011;34(3):187-197.

31. Pharmacovigilance & Introduction to Pharmacovigilance Risk Assessment Committee (PRAC). Zenodo. September 2025. https://doi.org/10.5281/zenodo.17224098.

32. Esslinger S, et al. Risk management plans: reassessment of safety concerns based on Good Pharmacovigilance Practices Module V (Revision 2) a company experience. J Pharm Health Care Sci. 2022;8(1):11.

33. Cai L, et al. Post- marketing surveillance framework of cell and gene therapy products in the European Union, the United States, Japan, South Korea and China: a comparative study. BMC Med. 2024;22(1):237.

34. World Health Organization. Pharmacovigilance Programme for Adverse Drug Reaction Monitoring. WHO Tech Rep Ser. 2002;908:50-70.

35. International Council for Harmonisation. ICH E2E Guidelines for Clinical Safety Data Management. ICH Expert Working Group; 2010.

36. European Medicines Agency. Guideline on Pharmacovigilance Planning. London: EMA; 2018.

37. U.S. Food and Drug Administration. Guidance for Industry: Pharmacovigilance Plan. Silver Spring, MD: FDA; 2011.

38. Central Drugs Standard Control Organization. Pharmacovigilance Programme of India Guidelines. CDSCO; 2019.

39. World Health Organization. Regulatory Challenges of Medicines in Developing Countries. WHO Tech Rep Ser. 2019;1037:45-67.