Pharmacovigilance and Post-Marketing Drug Withdrawals: National and International Experiences

Yuvraj Singh Rajput[1], Abhishek Mishra[2], Vaibhav Parouha[3], Neelima Goswami[4], R. B. Goswami[5]
[1,2,3,4,5]*Sagar Institute of Research Technology & Science-Pharmacy, Bhopal, Madhya Pradesh, India*

***Abstract*— Pharmacovigilance is an essential field dedicated to monitoring the safety and effectiveness of pharmaceuticals following their approval and market introduction. This discipline is crucial for identifying, evaluating, and mitigating adverse drug reactions (ADRs) that may not have been apparent during initial clinical trials. Even with rigorous pre-marketing assessments, certain medications can present unexpected risks, which may necessitate their removal from the market to protect public health on a global scale. The importance of pharmacovigilance cannot be overstated, as it serves as a safeguard for patients and health care systems alike. This comprehensive review delves into various international experiences concerning the withdrawal of drugs from the market as a result of pharmacovigilance efforts. This highlights the methodologies employed to detect adverse reactions, the regulatory frameworks that govern these processes, and notable instances of drug withdrawals that have occurred due to safety concerns. By examining these cases, the review underscores the challenges faced by pharmacovigilance systems worldwide, including issues related to data collection, reporting, and the integration of new technologies in monitoring drug safety. Furthermore, the document emphasizes the necessity of robust post-marketing surveillance and the application of advanced data mining techniques to enhance the detection of potential safety issues. It advocates for increased international collaboration among regulatory bodies, healthcare professionals, and pharmaceutical companies to improve pharmacovigilance practices. By sharing insights and recommendations, this review aims to contribute to the ongoing efforts to strengthen pharmacovigilance systems, ultimately leading to better patient safety and improved public health outcomes.**

***Index Terms*— Pharmacovigilance, Post-Marketing Surveillance, Drug Withdrawals, Adverse Drug Reactions (ADRs), Patient Safety, Regulatory Affairs, Signal Detection.**

I. INTRODUCTION

The process of bringing a drug from the laboratory to the patient encompasses several stages, including thorough pre-clinical and clinical evaluations that must be completed before a drug can receive market approval (Patel & Mehta, 2023). Despite these extensive testing phases, it is not uncommon for certain adverse effects to remain undetected until after the drug is made available to the public (Aronson et al., 2017). This gap in safety assessment is addressed by pharmacovigilance, which the World Health Organization (WHO) defines as the science and activities focused on the detection, assessment, understanding, and prevention of adverse effects or any drug-related issues (World Health Organization, 2020).

Pharmacovigilance serves as a crucial monitoring system for post-marketing safety, enabling the identification of rare, severe, or long-term adverse effects that may only become apparent following widespread use among varied populations (Dutta & Roy, 2024). The significance of pharmacovigilance was highlighted by historical incidents of drug safety failures, particularly the thalidomide crisis of the 1960s, which led to widespread birth defects across the globe and prompted the global implementation of systematic drug safety monitoring practices (WHO, 2020; Thomas & Narayanan, 2024). In the aftermath, pharmacovigilance has undergone significant evolution, incorporating advanced technologies and regulatory frameworks designed to effectively identify and manage drug-related risks (Kapoor & Desai, 2024).

Regulatory actions such as post-marketing drug withdrawals are vital tools in pharmacovigilance, particularly when the identified risks associated with a drug surpass its therapeutic benefits (Aronson et al.,

2017; Lakshmi & Narayanan, 2023). While these withdrawals are generally seen as unfavorable outcomes, they ultimately signify the effectiveness of pharmacovigilance efforts in safeguarding public health (Shukla & Goyal, 2024). The ability to withdraw a drug from the market underscores the importance of ongoing safety assessments even after a drug has been approved for use. This paper aims to review international experiences in pharmacovigilance concerning drug withdrawals, providing insights into the processes involved, the successes achieved, the challenges faced, and the future directions for ensuring drug safety on a global scale (Patel & Mehta, 2023; Thomas & Narayanan, 2024). By examining various case studies and regulatory frameworks, the paper seeks to illuminate the complexities of pharmacovigilance and its critical role in protecting patients. In conclusion, the ongoing evolution of pharmacovigilance is essential for maintaining drug safety in an ever-changing medical landscape (Ghosh et al., 2023). As new drugs are developed and introduced, the need for robust monitoring systems becomes increasingly important to ensure that any potential risks are promptly identified and addressed, thereby enhancing patient safety and trust in pharmaceutical interventions (WHO, 2020).

II. RATIONALE BEHIND THE WORK

The impetus for this review arises from the essential function of pharmacovigilance in safeguarding public health against the risks associated with unsafe medications (Shukla & Goyal, 2024). This discipline is crucial for monitoring the safety of pharmaceuticals post-approval, ensuring that any adverse effects are identified and addressed promptly (Dutta & Roy, 2024). Although clinical trials are instrumental in providing preliminary safety assessments, they often involve controlled environments and homogeneous populations (Patel & Mehta, 2023). In contrast, the real-world application of these drugs involves diverse patient groups with varying health conditions, genetic backgrounds, and environmental influences, all of which can significantly impact the safety and efficacy of medications.

Analysing international data regarding drugs that have been withdrawn from the market is vital for recognizing trends and understanding the regulatory actions taken in response to safety concerns (Aronson et al., 2017; Lakshmi & Narayanan, 2023). This analysis can reveal common factors that lead to drug withdrawals, thereby informing future regulatory practices and enhancing the overall safety framework. Identifying gaps in existing pharmacovigilance systems is crucial for developing more effective drug safety monitoring strategies (Kumar metal., 2024; WHO, 2023). By pinpointing these deficiencies, stakeholders can implement improvements that bolster the detection of adverse drug reactions and enhance the responsiveness of regulatory bodies. Ultimately, the insights gained from this review can contribute to the formulation of comprehensive strategies aimed at improving drug safety surveillance, promoting regulatory transparency, and ensuring that patient outcomes are optimized on a global scale (Patel & Mehta, 2023; Shukla & Goyal, 2024).

III. AIMS AND OBJECTIVES

The primary aim of this research is to evaluate the role and effectiveness of pharmacovigilance systems in identifying safety concerns that lead to the withdrawal of drugs from the market globally (Patel & Mehta, 2023). It seeks to analyze international experiences, regulatory responses, and the impact of pharmacovigilance activities on ensuring patient safety by preventing harm from adverse drug reactions discovered after market approval (Thomas & Narayanan, 2024). The specific objectives supporting this work are:

- To review and synthesize international case studies of drug withdrawals prompted by pharmacovigilance findings (Aronson et al., 2017).
- To understand the methodologies used in pharmacovigilance for detecting and assessing adverse drug reactions, including traditional reporting systems and advanced data mining techniques (Alomar, 2019; Tandon et al., 2024).
- To evaluate the timelines and regulatory decision-making processes involved in post-marketing drug withdrawals across various countries (Lakshmi & Narayanan, 2023).
- To identify challenges such as underreporting, regulatory inconsistencies, and resource limitations that affect pharmacovigilance effectiveness worldwide (Kumar et al., 2024;

WHO, 2023).

- To explore the importance of continuous education and awareness programs to enhance ADR reporting by healthcare professionals (Sharma & Patel, 2024).
- To examine the role of policy frameworks and international cooperation in harmonizing drug safety monitoring and withdrawal procedures (WHO, 2020).

IV. PLAN OF WORK AND METHODOLOGY

To execute the defined objectives systematically, the project followed a multi-stage operational framework encompassing literature synthesis, regulatory pathway tracking, and technology evaluation:

- Comprehensive Literature Review: Collection and tracking of scientific literature, regulatory publications, and documented case studies focusing on landmark drug safety profiles and global frameworks generated by the WHO, FDA, and EMA (WHO, 2020; US FDA, 2023; EMA, 2022).
- Data Collection on Pharmacovigilance Practices: Aggregation of post-marketing adverse event extraction patterns from active surveillance systems, electronic safety registries, and clinical safety dashboards (US FDA, 2023; Smith & Jones, 2022).
- Signal Detection and Causality Assessment: Methodological overview of reporting trends using mathematical data mining metrics, spontaneous report tracking, and specialized algorithm applications to differentiate background noise from verified signals (Alomar, 2019; Tandon et al., 2024; National Institute of Pharmaceutical Education and Research [NIPER], 2024).
- Review of International Regulatory Processes: Mapping out the exact legislative criteria, timeline intervals, and strategic milestones driving product recall workflows across divergent jurisdictions (Lakshmi & Narayanan, 2023).
- Challenges and Limitations Analysis: Identification of institutional bottlenecks, resource scarcity in developing markets, reporting gaps, and downstream structural fragmentation (Kumar et al., 2024; WHO, 2023).
- Assessment of Educational and Awareness Initiatives: Auditing academic, professional, and patient-focused capacity-building frameworks targeting clinical data quality improvements (Sharma & Patel, 2024).
- Technological Advances Integration: Investigation of emerging data ecosystems, focusing on the utility of machine learning models, natural language processing pipelines, and electronic medical record links in accelerating post-market safety discoveries (Chen & Li, 2023; Kapoor & Desai, 2024).

V. EVALUATION OF POST-MARKETING DRUG WITHDRAWALS

A critical component of pharmacovigilance is the tracking and execution of drug withdrawals when safety risks exceed therapeutic potential (Aronson et al., 2017). Table 1 catalogs prominent international and national drug recall instances, mapping out their therapeutic designations, regional details, and verified toxicity parameters.

No.	Drug Name (Brand)	Region / Origin	Primary Reason for Market Withdrawal	Toxicity Category
1	Rofecoxib (Vioxx)	USA / Global	Significant, verified elevation in long-term risk of myocardial infarction (heart attack) and stroke.	Cardiovascular Toxicity
2	Fenfluramine (Pondimin)	USA / Europe	Direct epidemiological association with severe heart valve disease and progressive pulmonary hypertension.	Cardiovascular / Pulmonary
3	Cerivastatin (Baycol)	Germany / USA	Elevated reports of acute, severe, and occasionally fatal rhabdomyolysis (skeletal muscle breakdown).	Musculoskeletal Toxicity
4	Tavaborol (Kerydin)	SA / Selected Regions	Strategic market risks and localized safety profiles; regional authorization remains highly variable.	Localized Cutaneous Risk
5	Cisapride (Propulsid)	USA / Global	Propensity to trigger severe, life-threatening cardiac arrhythmias and prolonged QT intervals.	Cardiovascular Arrhythmia

6	Nimesulide (Nimulid)	India / Select Markets	High incidence of severe hepatotoxicity, exhibiting prominent acute risks within pediatric patient demographics.	Hepatic Toxicity
7	Pioglitazone (Actos / Pioglit)	India	Statistical association with elevated risks of bladder cancer; temporarily banned, later heavily restricted.	Oncological Risk
8	Rosiglitazone (Avandia)	India (Licensed)	Post-market evidence confirming substantial increase in dangerous macro vascular cardiovascular events.	Cardiovascular Toxicity
9	Dextro propoxyphene	India / Global	High incidence of fatal cardio toxicity and severe toxic profile linked to accidental or intentional overdose.	Cardiovascular / Neuro-toxicity

Table 1: Comparative Profile of Major International and National Drug Withdrawals

VI. RESULTS AND DISCUSSION

Pharmacovigilance has proven to be an essential global health safeguard, identifying safety concerns with drugs post-approval that often necessitate their withdrawal from the market (Patel & Mehta, 2023; Shukla & Goyal, 2024). Both internationally and within India, numerous medicinal products have been withdrawn after post-marketing surveillance revealed serious adverse drug reactions (ADRs) not detected during clinical trials (Aronson et al., 2017; Verma et al., 2023).

6.1. International Pharmacovigilance Tracking

Several high-profile drug withdrawals worldwide illustrate the power and challenges of pharmacovigilance systems operating within mature regulatory frameworks (Thomas & Narayanan, 2024)

- Rofecoxib (Vioxx, USA): Withdrawn globally due to severe cardiovascular risks such as heart attack and stroke after widespread post-approval clinical use confirmed elevated hazards well beyond initial pre-market clinical trial findings (US FDA, 2023; Singh, 2025).
- Fenfluramine (Pondimin, USA/Europe): Clear epidemiological signals linking the agent to fatal pulmonary hypertension and valvular heart disease led to multi-country regulatory withdrawal mandates (EMA, 2022; Aronson et al., 2017).
- Cerivastatin (Baycol, Germany): Pulled completely from international markets following unexpected clusters of acute rhabdomyolyses resulting in severe muscle breakdown and secondary renal failures (Aronson et al., 2017; Singh, 2025).

6.2. Analysis of the Indian National Framework

India's pharmacovigilance landscape shows a trajectory marked by both significant structural progress and ongoing execution challenges (Ghosh et al., 2023; Pharmacovigilance Programme of India [PvPI], 2024). The Drugs Controller General of India (DCGI) alongside the Central Drugs Technical Advisory Board (DTAB) direct local safety responses, often operating via a mix of domestic adverse event data extraction and secondary alignment with foreign regulatory findings (Drugs Controller General of India [DCGI], 2023; Bhatt & Das, 2024). Local actions concerning agents like Nimesulide emphasize the unique demographic challenges encountered in India, where elevated pediatric hepatotoxicity profiles required aggressive legislative bans and clinical restrictions (Mishra & Singh, 2024; Verma et al., 2023).

Similarly, the regulatory path of Pioglitazone which involved an abrupt suspension followed by a structured reintroduction equipped with black-box warnings illustrates the complex socio-economic decisions required to balance oncological safety alerts against the widespread demand for accessible type-2 diabetes therapies (Mishra & Singh, 2024; Verma et al., 2023). Additionally, explicit cardio toxicity indicators drove the complete removal of Dextropropoxyphene and Rosiglitazone from active distribution channels (Verma et al., 2023; Singh, 2025).

Despite these interventions, the domestic ecosystem encounters distinct operational headwinds. The primary challenges include chronic clinical underreporting, the persistence of uncoordinated over-the-counter self-medication habits, and localized supply chain enforcement variances that permit restricted formulations to remain in active public circulation (Kumar et al., 2024; Shukla & Goyal, 2024; Indian Council of Medical Research [ICMR], 2023). Addressing these structural gaps represents a critical priority for optimizing local healthcare safety margins (Ghosh et al., 2023).

VII. CONCLUSION

The lessons learned from both international and Indian drug withdrawals highlight the critical importance of pharmacovigilance in safeguarding patient health on a global scale (Singh, 2025; Shukla & Goyal, 2024). As the landscape of pharmaceuticals continues to evolve, it becomes increasingly essential to adapt regulatory frameworks that can effectively respond to emerging challenges. This necessitates not only a robust system of monitoring and reporting adverse drug reactions but also the incorporation of advanced surveillance technologies that can detect potential safety issues in real time (Chen & Li, 2023; Kapoor & Desai, 2024).

Active engagement with various stakeholders, including healthcare professionals, pharmaceutical companies, and regulatory bodies, is vital for optimizing drug safety monitoring (WHO, 2020). Collaborative efforts can lead to the sharing of critical data and insights, which can inform better decision-making processes regarding drug approvals and withdrawals (World Health Organization Collaborating Centre for International Drug Monitoring, 2023). Furthermore, the integration of patient feedback into pharmacovigilance systems can provide a more comprehensive understanding of drug effects in diverse populations. This multifaceted approach not only strengthens the regulatory framework but also builds public trust in the healthcare system, as patients feel more secure knowing that their safety is a priority (Shukla & Goyal, 2024).

Strengthening collaboration between countries and within India's healthcare ecosystem is essential for effectively mitigating the risks posed by harmful drugs (WHO, 2023; PvPI, 2024). By establishing international partnerships and sharing best practices, nations can create a more unified front against unsafe medications. In India, enhancing communication among healthcare providers, regulatory agencies, and the pharmaceutical industry can lead to more efficient identification and management of drug-related risks (Bhatt & Das, 2024; Ghosh et al., 2023). Ultimately, these concerted efforts will ensure that both global and local populations have access to the safest therapeutic options, thereby improving health outcomes and fostering a more resilient healthcare environment.

REFERENCES

[1] M. J. Alomar, "Pharmacovigilance data mining and drug withdrawals," *Saudi Pharmaceutical Journal*, vol. 27, no. 4, pp. 492–499, 2019.

[2] J. K. Aronson *et al*., "Post-marketing drug withdrawals due to safety concerns: A review," *Pharmacoepidemiology and Drug Safety*, vol. 26, no. 8, pp. 871–878, 2017.

[3] Bhatt and S. Das, "Drug safety monitoring and regulatory updates in India," *Journal of Pharmacy and Bioallied Sciences*, vol. 16, Suppl. 1, pp. S45–S52, 2024.

[4] X. Chen and Q. Li, "Machine learning applications in pharmacovigilance for signal detection," *Journal of Biomedical Informatics*, vol. 139, Art. no. 104302, 2023.

[5] Drugs Controller General of India, *Guidelines on Pharmacovigilance and Drug Safety*. New Delhi, India: CDSCO Publications, Ministry of Health, 2023.

[6] S. Dutta and A. Roy, "Clinical significance of post-marketing surveillance," *Journal of Pharmaceutical Sciences*, vol. 113, no. 2, pp. 311–319, 2024.

[7] European Medicines Agency, *Regulatory Frameworks for Drug Withdrawals in the EU*. Science Strategy Division, 2022.

[8] R. Ghosh *et al*., "Pharmacovigilance in India: Past, present and future," *Indian Journal of Pharmacology*, vol. 55, no. 3, pp. 178–187, 2023.

[9] Indian Council of Medical Research, *Guidelines on Adverse Drug Reaction Monitoring*. New Delhi, India: ICMR Scientific Publications, 2023.

[10] International Society of Pharmacovigilance, *Proceedings of the 23rd Annual Meeting*, 2023.

[11] S. Kapoor and B. Desai, "Integration of technology in pharmacovigilance: Indian perspective," *Journal of Pharmacy and Technology*, vol. 17, no. 2, pp. 88–95, 2024.

[12] S. Kumar *et al*., "Challenges in pharmacovigilance practices in low and middle-income countries," *Indian Journal of Pharmacology*, vol. 56, no. 1, pp. 34–41, 2024.

[13] V. Lakshmi and S. Narayanan, "Post-marketing drug withdrawal: International regulatory perspectives," *Regulatory*

Toxicology and Pharmacology, vol. 142, Art. no. 105431, 2023.

[14] P. Mishra and V. Singh, "Review on banned drugs in India," *International Journal of Pharmaceutical Sciences and Research*, vol. 15, no. 4, pp. 1302–1311, 2024.

[15] National Institute of Pharmaceutical Education and Research, *Pharmacovigilance Research Methods: Academic Handbook*. NIPER Publications, 2024.

[16] H. Patel and P. Mehta, "Overview of pharmacovigilance and drug withdrawals: A global scenario," *Journal of Global Pharmaceutical Technology*, vol. 15, no. 6, pp. 45–56, 2023.

[17] Pharmacovigilance Programme of India, *Annual Report 2023–24*. Ministry of Health and Family Welfare, Government of India, 2024.

[18] P. Sharma and D. Patel, "Enhancing healthcare professional reporting of ADRs: Educational interventions," *Journal of Pharmacy Practice*, vol. 37, no. 2, pp. 245–252, 2024.

[19] Shukla and R. Goyal, "Role of pharmacovigilance in patient safety: Indian insights," *Indian Journal of Medical Research*, vol. 159, no. 2, pp. 145–154, 2024.

[20] R. Singh, "Case studies of major post-marketing drug withdrawals: Lessons learned," *Indian Journal of Clinical Medicine*, vol. 16, no. 2, pp. 112–120, 2025.

[21] M. Smith and L. Jones, "Pharmacovigilance methods in post-marketing surveillance," *British Journal of Clinical Pharmacology*, vol. 88, no. 9, pp. 4105–4116, 2022.

[22] K. R. Stansil, "Formulation and evaluation of herbal loofah soap incorporating neem oil, peppermint, and aloe vera," *International Journal of Pharmacy and Pharmaceutical Sciences*, vol. 16, no. 5, pp. 89–94, 2024.

[23] R. Tandon *et al*., "Signal detection in pharmacovigilance: Tools and techniques," *Journal of Pharmacovigilance and Drug Safety*, vol. 21, no. 1, pp. 12–22, 2024.

[24] K. Thomas and S. Narayanan, "International experiences in drug withdrawals due to ADRs," *Therapeutic Advances in Drug Safety*, vol. 15, Art. no. 2042098624123456, 2024.

[25] U.S. Food and Drug Administration, *Adverse Event Reporting System and Post-Marketing Safety Surveillance*. Center for Drug Evaluation and Research, FDA Publications, 2023.

[26] D. Verma *et al*., "Pharmacovigilance and regulatory actions in India: Case studies," *Indian Journal of Pharmacology*, vol. 55, no. 4, pp. 289–296, 2023.

[27] World Health Organization, *Pharmacovigilance: Ensuring Drug Safety Worldwide*, WHO Technical Report Series No. 1024. Geneva, Switzerland: WHO, 2020.

[28] World Health Organization, *Technical Report on Pharmacovigilance Strengthening in Low and Middle-Income Countries*. Geneva, Switzerland: WHO Department of Medicines Safety, 2023.

[29] World Health Organization Collaborating Centre for International Drug Monitoring, *Uppsala Monitoring Centre Annual Scientific Reports*. UMC Press, 2023.