International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2595-2601 www.ijprajournal.com ISSN: 2456-4494

A Report on-From Clinical Trials To Post Marketing Surveillance: The Evaluation Of Safety Data Generation In Pharmacovigilance

Prof. (Dr.)Mohd.Wasiullah [1] , Prof. (Dr.)Piyush Yadav[2] , Dr. Shashikant Maury[3]*, Asst. Prof. Mohit Vishwakarma[4], Akash Yadav[5]

Date of Submission: 25-04-2025 Date of Acceptance: 05-05-2025

ABSTRACT
Pharmacovigilance is a critical field dedicated to the science and activities related to the detection, assessment, understanding, and prevention of adverse drug reactions (ADRs) and other drug-related problems. This report provides a comprehensive overview of pharmacovigilance, emphasizing its importance in improving patient safety and ensuring that the benefits of medicinal products outweigh their risks. The report outlines the goals of pharmacovigilance, including the detection of ADRs, evaluation of risk-benefit profiles, prevention of harm, and provision of evidence for regulatory decisions.The transition from clinical trials to post-marketing surveillance (PMS) is highlighted as a crucial phase in pharmacovigilance, where safety data is generated in real-world settings. While clinical trials offer valuable insights into drug safety, they often involve controlled populations and limited durations, which may not capture rare or long-term adverse effects. PMS addresses these limitations by collecting data from diverse patient populations, allowing for ongoing safety monitoring and risk management.The report discusses various methods of safety data collection in PMS, including spontaneous reporting systems, epidemiological studies, and registries. It also examines the challenges faced in PMS, such as underreporting of ADRs and data quality issues. Advanced statistical methods and data analytics, including Bayesian analysis and machine learning, are explored as tools for signal detection and risk assessment.

KEYWORD: Pharmacovigilance,Adverse Drug Reactions,Drug Safety, Post-Marketing Surveillance, Safety Data, Clinical Trials.

I. INTRODUCTION

Pharmacovigilance is the science focused on detecting, assessing, understanding, and preventing adverse drug effects and other medication-related issues. Its main objective is to enhance patient safety by monitoring the safety of medicinal products, particularly after they are approved and used in the general population. While clinical trials provide essential data on a drug's efficacy and safety, they involve controlled conditions and limited populations, often missing rare or long-term adverse effects. The need for ongoing safety monitoring became evident after incidents like the thalidomide tragedy in the 1960s, which spurred the development of global pharmacovigilance systems. Today, pharmacovigilance is a vital part of regulatory frameworks, ensuring that medications remain safe throughout their lifecycle. It involves collaboration among pharmaceutical companies, regulatory agencies, healthcare professionals, and patients. A key component is the post-marketing surveillance of drugs, which enables the continuous collection and analysis of safety data in real-world settings to identify and manage risks promptly.

❖ Definition and Importance

Pharmacovigilance, as defined by the World Health Organization (WHO), is the science and activities related to the detection, assessment, understanding, and prevention of adverse effects or other drug-related problems. This includes adverse drug reactions (ADRs), which are harmful and unintended effects occurring at normal therapeutic doses. ADRs can range from mild issues like rashes to severe outcomes such as organ damage or death.Pharmacovigilance plays a vital role in ensuring that medicines remain safe and effective after market approval. According to the U.S. FDA, it is essential for ensuring that a drug's benefits continue to outweigh its risks. Continuous safety monitoring helps detect new or rare ADRs, prompting timely interventions like label updates or drug withdrawals. Additionally, pharmacovigilance builds public confidence in healthcare systems by keeping patients and

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2595-2601 www.ijprajournal.com ISSN: 2456-4494

providers informed of potential risks. It also supports better clinical decision-making by equipping healthcare professionals with current safety information about medications.

❖ **Goals of Pharmacovigilance**

Pharmacovigilance aims to ensure drug safety through various key goals. These include the detection of previously unrecognized adverse drug reactions (ADRs), especially once a drug is used by a broader population. It also involves evaluating the drug's risk-benefit profile and taking necessary actions—such as updating labels or withdrawing the drug—to prevent harm. Pharmacovigilance supports regulatory decisions by providing vital safety data and contributes to improving drug development by identifying early safety concerns. Overall, it plays a critical role in safeguarding public health and enhancing the effectiveness and safety of medicinal products throughout their lifecycle.

❖ **Scope of the Report**

This report evaluates how safety data is generated and used in pharmacovigilance, focusing on the transition from clinical trials to post-marketing surveillance (PMS). It highlights the limitations of clinical trials and emphasizes real-world data collection, signal detection methods, and regulatory involvement. The report also examines challenges and limitations in current pharmacovigilance practices, aiming to ensure the continuous safety of medicinal products throughout their lifecycle.

❖ **Transition from Clinical Trials to Post-Marketing Surveillance**

Post-marketing surveillance (PMS) addresses the limitations of clinical trials by monitoring drug safety in broader, real-world populations. Unlike controlled trials, PMS captures diverse patient responses, comorbidities, and off-label uses. It utilizes spontaneous reports, observational studies, and registries to detect new safety concerns. Pharmacovigilance plays a critical role in evaluating these data, identifying emerging risks, and implementing measures to protect public health after a drug is marketed.

❖ **Impact on Patient Safety**

Pharmacovigilance ensures patient safety by identifying and managing drug risks through clinical trials and post-marketing surveillance. It detects adverse reactions missed in trials and triggers regulatory actions like label changes, warnings, or market withdrawal. By providing timely safety information, pharmacovigilance helps healthcare providers and patients make informed decisions, ultimately reducing harm and improving patient outcomes.

II. BASICS OF PHARMACOVIGILANCE

❖ **Pharmacovigilance and its Role in Drug Safety**

Pharmacovigilance focuses on the detection, assessment, understanding, and prevention of adverse drug reactions (ADRs) or other drug-related issues. It ensures that the benefits of medications outweigh their risks, playing a crucial role throughout a drug's lifecycle. Post-marketing surveillance identifies safety concerns not detected in clinical trials, as drugs are used by broader, more diverse populations, often with co-existing conditions. Continuous monitoring minimizes public health risks by managing adverse events effectively.

❖ **International Perspective (WHO, FDA, EMA)**

Key global organizations play pivotal roles in pharmacovigilance:

- **WHO**: Leads global drug safety monitoring through the Uppsala Monitoring Centre (UMC), promoting safety reporting and harmonization of practices worldwide.
- **FDA**: Manages the MedWatch program to monitor drug safety in the U.S. and collaborates internationally on risk-benefit evaluations.
- **EMA**: Oversees drug safety in the EU through the Pharmacovigilance Risk Assessment Committee (PRAC), ensuring medicines are safe and effective in the market.

❖ **Definitions and Terminology**

Understanding critical terms in pharmacovigilance is essential:

- **ADRs**: Unintended harmful responses to drugs.
  - **Type A (Augmented)**: Dose-dependent and predictable.
  - **Type B (Bizarre)**: Unpredictable, often immune-mediated.
- **SADR**: Serious adverse drug reactions leading to death, hospitalization, or disability.
- **Signal**: Safety concerns detected from ADR reports.

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2595-2601 www.ijprajournal.com ISSN: 2456-4494

- **Causality Assessment**: Process of determining if a drug caused an ADR.

❖ **Types of Safety Data in Pharmacovigilance**

Pharmacovigilance utilizes various data types:

- **Preclinical Data**: Animal and laboratory studies predicting toxicity.
- **Clinical Trial Data**: Safety data from controlled trials.
- **Post-Market Data**: Real-world data from healthcare providers and patients.
- **Spontaneous Reporting**: Voluntary reporting systems for ADRs.
- **Registry and Observational Data**: Long-term safety data for chronic conditions.

❖ **Adverse Drug Reactions (ADRs)**

ADRs are categorized by severity:

- **Mild**: Self-limiting reactions (e.g., rash).
- **Moderate**: Reactions requiring medical intervention.
- **Severe**: Life-threatening reactions requiring immediate attention.

❖ **Risk Management**

Risk management aims to minimize drug risks through:

- **Risk Minimization**: Label changes, restricted use, or safety monitoring.
- **Risk Communication**: Informing stakeholders about drug safety.
- **Risk Assessment**: Ongoing evaluation of a drug's safety profile.

❖ **Signal Detection and Risk Assessment**

Signal detection involves identifying potential safety concerns using statistical methods. Once a signal is detected, a risk assessment evaluates its seriousness and frequency, determining necessary regulatory actions.

❖ **Role of National Regulatory Authorities**

National regulatory authorities, such as the FDA, EMA, and MHRA, implement pharmacovigilance programs, monitor ADRs, and collaborate with international bodies to ensure drug safety. They provide guidance, enforce safety regulations, and support risk management strategies.

III. SAFETY DATA GENERATION IN CLINICAL TRIALS

The generation of safety data in clinical trials is a cornerstone of evaluating new treatments and therapies. Safety data is critical for determining the potential risks and benefits of a drug or medical intervention before it can be approved for general use. Clinical trials are designed to gather extensive data about the safety, efficacy, and pharmacokinetics of a treatment. This chapter will provide a comprehensive overview of the process of safety data generation in clinical trials, detailing the differences between pre-clinical and clinical safety data, the phases of clinical trials, clinical trial design, and the challenges faced during safety data collection..

❖ **Pre-Clinical vs. Clinical Safety Data**

Before clinical trials, pre-clinical safety data is generated through animal and laboratory testing to assess toxicity and pharmacological properties. Pre-clinical tests help determine safe starting doses and monitor potential adverse effects. However, these models may not accurately predict human safety due to differences in metabolism and immune responses. Clinical trials are essential for confirming safety in humans, accounting for genetic diversity and other variables.

❖ **Phases of Clinical Trials (I-IV)**

Clinical trials are conducted in four phases:

- **Phase I**: Focuses on safety and pharmacokinetics, involving 20-100 healthy volunteers to determine the maximum tolerated dose (MTD) and initial safety profile.
- **Phase II**: Involves 100-300 patients to assess efficacy and identify the optimal dose while monitoring safety.
- **Phase III**: Includes 1,000-3,000 participants, providing definitive evidence on safety and efficacy, often comparing the drug with existing treatments or a placebo.
- **Phase IV**: Post-marketing trials collect safety data from a larger population to detect rare or long-term side effects that may not have been seen in earlier phases.

❖ **Clinical Trial Design and Monitoring**

Key components of clinical trial design include:

- **Randomization**: Participants are randomly assigned to treatment or control groups to reduce bias.
- **Blinding**: In double-blind trials, neither the participants nor the researchers know who receives the treatment, minimizing bias.

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2595-2601 www.ijprajournal.com ISSN: 2456-4494

- **Endpoints**: Safety endpoints, including adverse events (AEs) and serious adverse events (SAEs), provide critical information on a drug's risks.
- **Monitoring**: An independent data monitoring committee reviews safety data and makes recommendations on the trial's progression.

❖ **Randomized Controlled Trials (RCTs)**

RCTs are the gold standard in clinical research, minimizing bias by randomly assigning participants to either a treatment or placebo group. They are essential for assessing causality and ensuring the validity of safety data.

❖ **Adverse Event Reporting and Systems**

All adverse events must be reported to identify patterns and assess risks. Reporting systems like MedDRA standardize the classification of AEs, improving consistency and analysis across studies.

❖ **Limitations of Safety Data**

Clinical trials face limitations such as small sample sizes, which may miss rare adverse events, short trial durations that cannot detect long-term effects, and a homogeneous participant pool that may not reflect the broader population's safety profile. These limitations highlight the importance of post-marketing surveillance.

IV. POST-MARKETING SURVEILLANCE (PMS)

❖ **Introduction to Post-Marketing Surveillance**

Post-Marketing Surveillance (PMS), or Phase IV clinical trials, involves monitoring the safety and effectiveness of pharmaceutical products after they are released to the market. Unlike pre-market trials, which occur in controlled environments with limited participants, PMS gathers real-world data from diverse populations. This phase is crucial for detecting adverse drug reactions (ADRs) that may not have been identified in earlier trials due to their limited scope or duration.

❖ **Transition from Clinical Trials to Real-World Data**

While clinical trials assess a drug's efficacy and safety under controlled conditions, they often involve strict participant criteria and short durations. PMS bridges this gap by collecting data from the general population, including individuals with comorbidities, the elderly, and those on multiple medications, helping identify rare or long-term side effects and assessing the overall benefit-risk profile of a drug.

❖ **Phases of Post-Marketing Surveillance (Phase IV)**

Phase IV begins once a drug is approved and marketed. It includes:

- **Ongoing Safety Monitoring**: Continuously assessing the safety profile of the drug.
- **Efficacy Studies**: Evaluating the long-term effectiveness of the drug.
- **Risk Management**: Identifying potential risks and implementing strategies to minimize them.
- **Regulatory Actions**: Adjusting drug labeling, usage guidelines, or withdrawing the drug if safety concerns arise.

❖ **Methods of Safety Data Collection in PMS**

Several methods are used to collect safety data during PMS:

- **Spontaneous Reporting Systems**: Voluntary systems where healthcare professionals and patients report ADRs. Examples include:
  - **VigiBase**: A global database managed by the WHO.
  - **FDA FAERS**: Operated by the U.S. FDA for ADR and medication error reports.
  - **EudraVigilance**: Managed by the European Medicines Agency (EMA) for suspected ADRs in the EU.
- **Epidemiological Studies**: These studies observe patterns and causes of ADRs in populations, helping identify risk factors and evaluate risk minimization strategies.
- **Observational Studies**: Including cohort studies (following individuals over time) and case-control studies (comparing those with and without specific ADRs).
- **Registries and Databases**: Collect data on specific diseases or treatments, assisting in long-term safety monitoring and identifying rare ADRs.

❖ **Global Pharmacovigilance Systems**

International systems facilitate safety data collection, such as:

- **VigiBase**: A WHO database enabling early detection of drug-related issues.
- **FDA FAERS**: Supports FDA's safety surveillance of approved drugs.
- **EMA EudraVigilance**: Assists the EU in monitoring ADRs.

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2595-2601 www.ijprajournal.com ISSN: 2456-4494

❖ **Challenges in Post-Marketing Surveillance**

PMS faces several challenges:

- **Underreporting of Adverse Events**: Healthcare providers may underreport due to lack of time, uncertainty about causality, or perceived lack of incentives.
- **Data Quality and Completeness**: Incomplete reports may hinder accurate safety assessments.
- **Data Privacy**: Ensuring patient confidentiality, as per regulations like GDPR.
- **Signal Detection and Risk Management**: Sophisticated methods are needed to detect safety signals and implement effective risk management strategies.

❖ **Signal Detection Methods**

Advanced statistical techniques, such as Bayesian Confidence Propagation Neural Network (BCPNN), Proportional Reporting Ratios (PRRs), and Empirical Bayes Geometric Mean (EBGM), are used to identify safety signals in large datasets.

V. EVALUATION OF SAFETY DATA GENERATION

❖ **Importance of Safety Data in Pharmacovigilance**

Safety data plays a crucial role in the continuous monitoring of pharmaceutical products. It helps evaluate the safety profile of drugs post-market, ensuring patient protection and regulatory compliance. This data is essential for identifying adverse drug reactions (ADRs), updating treatment guidelines, and improving drug safety. Pharmacovigilance ensures public health by gathering, analyzing, and interpreting safety data, which aids in making decisions regarding labeling, additional studies, and market withdrawals.

❖ **Enhancing Public Health Safety**

Post-marketing surveillance (PMS) provides real-world evidence of drug safety, monitoring adverse effects in a broader population, including individuals who were excluded from clinical trials. It helps detect rare or long-term ADRs and minimize health risks. PMS ensures the benefits of a drug outweigh the risks by continuously monitoring safety throughout its lifecycle.

❖ **Risk-Benefit Assessment**

Risk-benefit assessment evaluates a drug's therapeutic benefits against its potential risks. Regulatory authorities, such as the FDA and EMA, use PMS data to assess whether a drug's risks remain acceptable relative to its benefits. If risks become significant, actions like label changes or market withdrawal may be taken. The aim is to ensure the drug provides more benefit than harm.

❖ **Data Quality and Integrity**

The accuracy, completeness, and consistency of safety data are vital for effective pharmacovigilance. Poor or incomplete data can lead to wrong conclusions, affecting patient safety. Standardized reporting systems like the FDA's FAERS, EMA's EudraVigilance, and WHO's VigiBase ensure data integrity, prevent data manipulation, and enhance the reliability of safety evaluations.

❖ **Ensuring Data Accuracy and Completeness**

Accurate and complete data ensures early identification of risks. Inaccurate or incomplete ADR reports can delay detection, prolonging exposure to harmful drugs. To enhance data accuracy, regulatory agencies promote structured reporting systems, encourage healthcare professionals' participation, and use advanced methods like Bayesian analysis and machine learning to detect risk patterns.

❖ **Role of Health Professionals and Patients in Reporting**

Healthcare professionals and patients are critical in generating safety data. They help identify ADRs, providing valuable insights into drug safety. However, underreporting is common due to time constraints, lack of training, or uncertainty about causality. Addressing these issues through education, incentives, and simplified reporting can improve data quality.

❖ **Analyzing Safety Data from Clinical Trials and PMS**

Clinical trials provide initial insights into a drug's safety, but they are often limited by controlled conditions and sample size. PMS, however, offers a broader perspective by monitoring drug safety in a diverse, real-world population. Integrating clinical trial and PMS data provides a comprehensive understanding of a drug's safety profile.

❖ **Comparative Analysis of Data from Clinical Trials vs. Post-Marketing**

Clinical trials and PMS offer complementary safety data. Trials focus on

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2595-2601 www.ijprajournal.com ISSN: 2456-4494

identifying risks in controlled environments, while PMS captures rare or long-term ADRs in a larger population. A comparative analysis helps identify discrepancies and potential safety issues not detected during trials, prompting necessary regulatory actions.

❖ **Statistical Methods in Safety Evaluation**

Various statistical methods are used in safety evaluation, including Bayesian analysis, Proportional Reporting Ratios (PRRs), and Empirical Bayes Geometric Mean (EBGM). These techniques help detect ADR signals early, ensuring that risks are effectively communicated and managed

❖ **Data Mining and Advanced Analytics**

Data mining and advanced analytics, such as machine learning and Bayesian analysis, have revolutionized safety data evaluation. These methods can uncover hidden associations between drugs and ADRs, enabling early identification of potential safety concerns and ensuring timely intervention.

❖ **Regulatory Actions Based on Safety Data**

Regulatory agencies can take actions based on safety data, such as issuing drug warnings, market withdrawals, or recalls. In cases of significant risks, drugs may be recalled, and labeling changes may be required to communicate new safety information effectively

.

❖ **Risk Communications**

Risk communication is a vital part of pharmacovigilance. Regulatory agencies issue drug warnings and black box warnings to alert healthcare providers and patients about serious adverse effects. Effective risk communication ensures that safety information is promptly shared, helping prevent adverse events.

❖ **Drug Recalls and Market Withdrawals**

When a drug is found to be unsafe or ineffective, regulatory bodies may recall it from the market. Recalls are initiated when a drug poses significant risks, such as severe side effects or incorrect labeling, to protect public health.

❖ **Labeling Changes**

New safety information can lead to changes in a drug's labeling, such as the addition of warnings or contraindications. Labeling updates ensure that healthcare providers and patients are informed about potential risks and side effects, enhancing safety and informed decision-making.

VI. CONCLUSION

In conclusion, pharmacovigilance plays a critical role in ensuring the safety and efficacy of pharmaceutical products throughout their lifecycle. From the early stages of clinical trials to the post-marketing phase, pharmacovigilance continually monitors and assesses the risk-benefit profile of drugs, identifying potential adverse drug reactions (ADRs) that may not have been detected during pre-market trials. While clinical trials offer vital data on the safety and efficacy of drugs under controlled conditions, they are limited in scope and duration, often failing to capture rare, long-term, or population-specific ADRs. This is where post-marketing surveillance (PMS) becomes indispensable, providing real-world evidence by monitoring drugs once they are widely used by the general population. PMS involves diverse data collection methods such as spontaneous reporting, registries, observational studies, and epidemiological studies, all of which help uncover adverse events that may not have appeared in clinical trials. This phase allows for continuous safety monitoring, risk management, and the adjustment of drug labels or even withdrawal of drugs from the market when significant safety issues arise. However, challenges such as underreporting of ADRs, incomplete data, and ensuring patient confidentiality remain hurdles in effective pharmacovigilance. Addressing these issues requires the active involvement of healthcare professionals, patients, regulatory authorities, and pharmaceutical companies in maintaining data accuracy and completeness.Moreover, advanced statistical methods and data analytics, such as Bayesian analysis, machine learning, and signal detection algorithms, have revolutionized the way safety data is analyzed. These techniques help identify safety signals early, ensuring that the risks associated with a drug are recognized promptly, allowing for quick regulatory action, including drug warnings, recalls, or label modifications. Regulatory bodies such as the WHO, FDA, and EMA play a vital role in standardizing pharmacovigilance practices worldwide, ensuring that safety data is shared and analyzed globally to protect public health.Ultimately, pharmacovigilance is not just about identifying risks but also about ensuring that the benefits of drugs outweigh the potential harms.

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2595-2601 www.ijprajournal.com ISSN: 2456-4494

REFERENCE

[1]. Edwards, I. R., & Aronson, J. K. (2000). Adverse drug reactions: Definitions, diagnosis, and management. The Lancet, 356(9237), 1255-1259.
[2]. World Health Organization (WHO). (2002). Pharmacovigilance: A summary of the WHO initiative. Drug Safety, 25(5), 287-295.
[3]. European Medicines Agency. (2017). Good Pharmacovigilance Practices (GVP). European Medicines Agency.
[4]. U.S. Food and Drug Administration (FDA). (2019). Pharmacovigilance: The role of safety monitoring in drug regulation. FDA Consumer Magazine, 53(4), 14-17.
[5]. Bate, A., & Lindquist, M. (2008). Pharmacovigilance: Signal detection and the evaluation of safety data. British Journal of Clinical Pharmacology, 65(1), 48-56.
[6]. Leong, J., & Tien, G. (2015). Post-marketing surveillance and the role of pharmacovigilance in public health. Pharmacoepidemiology and Drug Safety, 24(3), 304-310.
[7]. Temple, R., & Thorsen, N. (2006). Clinical Trial Design and Safety. *Journal of Clinical Pharmacology*, 46(3), 309-317.
[8]. Zhang, X., Zhang, Y., Ye, X., Guo, X., Zhang, T., & He, J. (2016).
[9]. Alomar, M. J. (2014).* Saudi Pharmaceutical Journal, 22(2), 83–94.
[10]. Hazell, L., & Shakir, S. A. W. (2006). Drug Safety, 29(5), 385–396.
[11]. Edwards, I. R., & Aronson, J. K. (2000). Adverse drug reactions: Definitions, diagnosis, and management. Drug Safety, 22(4), 225-233.
[12]. . Edwards, I. R., & Aronson, J. K. (2000). Adverse drug reactions: definitions, diagnosis, and management. *The Lancet*, 356(9237), 1255–1259.
[13]. . Hazell, L., & Shakir, S. A. W. (2006). Under-reporting of adverse drug .
[14]. Pahwa, M., & Dabbous, Z. (2016). Randomized Controlled Trials: Methodology and Reporting Standards. Journal of Clinical Research, 8(4), 135-145.
[15]. Moore, T. J., & Cohen, M. R. (2014). The role of post-marketing surveillance in pharmacovigilance. Pharmacological Research, 88, 5-16.
[16]. Hazell, L., & Shakir, S. A. (2006). Underreporting of adverse drug reactions: A systematic review. Drug Safety, 29(5), 385-396.
[17]. Chung, S. C., & Lee, Y. J. (2013). Signal detection in pharmacovigilance: Methods and applications. Journal of Clinical Pharmacology, 53(12), 1269-1284.
[18]. Poluzzi, E., & Punzi, E. (2013). Signal detection and data mining in pharmacovigilance: New insights and techniques. Pharmacological Research, 68(6), 199-208.
[19]. Bates, D. W., & Boxerman, S. B. (2003). The importance of accurate and complete safety data in pharmacovigilance. Journal of the American Medical Association, 289(1), 14-22.
[20]. Loke, Y. K., & Price, D. (2012). Post-marketing surveillance: A global approach to the safe use of medicines. British Journal of Clinical Pharmacology, 74(2), 204-216.
[21]. Shakir, S. A. W., & Robinson, R. (2002). Pharmacovigilance: A priority for public health. Drug Safety, 25(6), 429-440.
[22]. Herxheimer, A., & Peters, D. (2005). Pharmacovigilance: A major tool for safeguarding public health. Pharmaceutical Policy and Law, 7(2), 61-70.