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Review article

Pharmacovigilance: strengthening drug safety through monitoring and reporting

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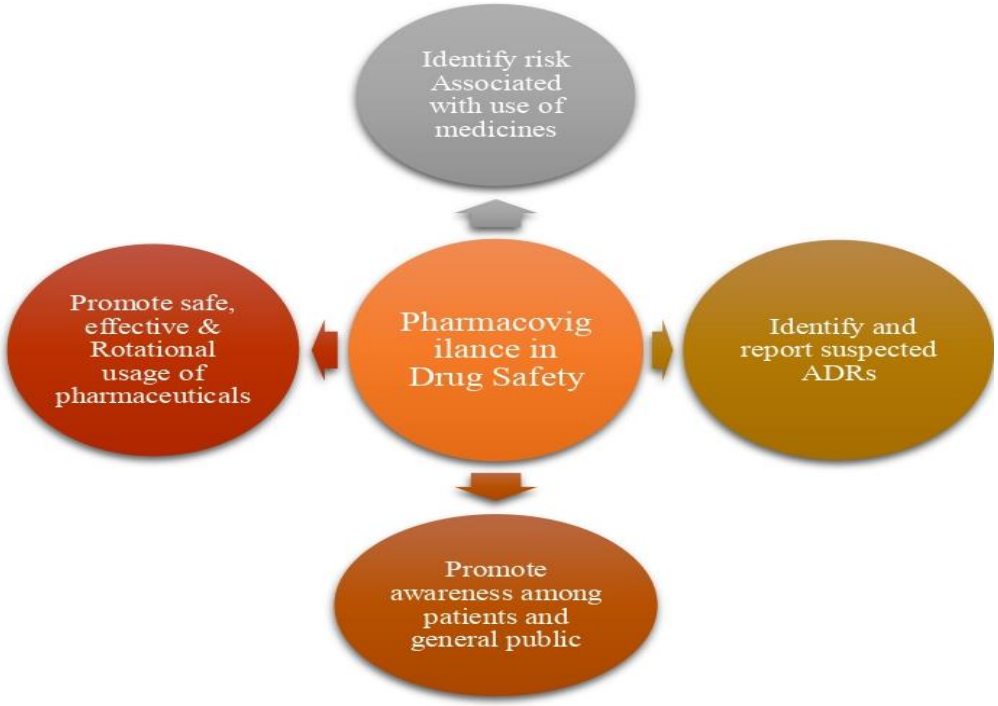
ABSTRACT

Pharmacovigilance is essential to clinical research and is a key element in guaranteeing the safety of medications. It is described as the study and practice of recognizing, evaluating, understanding, and averting adverse medication reactions or other problems.The goal of pharmacovigilance, a continuous monitoring procedure, is to identify and address safety concerns with medications that are currently on the market. The review's primary focus is on the purpose, necessity, and role of medicine regulation. Lately drug surveillance has been limited, mostly to identify previously undiscovered or unfavorable drug events that are not well understood. A lot of drug safety facilities are currently striving to monitor medication safety in this universal arena; yet, at the turn of the decade, medication surveillance faces significant obstacles in the area of improved drug administration and control. Pill security, global monitoring centers and their role, reach, necessity, cooperation, and collaboration will all be covered in this study.



Keywords: Pharmacovigilance, Medication safety, Drug surveillance, Clinical research, Global monitoring.

INTRODUCTION

Pharmacovigilance is an important and crucial part of medical research. Studies on safety and post-marketing pharmacovigilance are both essential throughout the product lifecycle. What is known about pharmacovigilance's advantages, hazards, difficulties, and prospects in Indian medicine? The pharmaceutical science that focuses on identifying, assessing, understanding, and preventing side effects is known as pharmacovigilance. The goals and role of pharmacovigilance in the regulation of drugs and their partners are the main focus here. Covering the adverse effects of drugs, both immediate and the future. Pharmacovigilance is still very new in India, and not much is known about it. Not much has been accomplished in India in the field of pharmacovigilance, despite significant improvements occurring in western nations. Pharmacovigilance is not new to India; in fact, it has existed since 1998. India made the decision to join the Uppasla centre in order to monitor undesirable events. The media and regulatory bodies have recognized the value of pharmacovigilance, and consumers are now more knowledgeable about the advantages and disadvantages of medications. One definition of an adverse event is "any unfavorable medical event that may occur during drug treatment but does not necessarily have a relationship with its use." An adverse drug reaction is any unpleasant, unanticipated, and undesirable side effect of a medication that occurs at a dosage used in humans for evaluation, therapy, prevention, or adjustment of physiological function. The spontaneous reporting of adverse drug reactions and occurrences is one of the most important ways to gather safety data for quick identification. Numerous Indian businesses have been investing more in R&D in recent years, strengthening their capacity to conduct internal research to develop and market innovative drugs [1]. There are several challenges that Pharmacovigilance must overcome in order to improve healthcare systems around the world. The pharmaceutical industry versus public health, web-based sales and information, globalization, economic growth, monitoring of current medications, emerging and developing nations, attitudes and perceptions regarding benefits and drawbacks, results, and impacts, and more are some of the main challenges [2].

Government Pharmacovigilance systems were established throughout Europe in anticipation of the thalidomide tragedy. In the 1950s, a dose of was used to treat nausea and induce sleep in expectant mothers. After noticing an unusually high number of newborns with phocomelia, two doctors the reproductive harm of this drug was initially suggested in 1961 by Drs. McBride from Australia and Lenz in Germany [3-5]. A retrospective investigation conducted in 1973 verified the link between thalidomide consumption during pregnancy and congenital birth defects [6]. During the pandemic, pharmacovigilance initiatives for COVID-19 vaccinations have been crucial in addressing public health issues. In order to attain herd immunity through mass vaccination, pharmacovigilance readiness has received much attention [7]. In order to ensure thorough safety assessment, a comprehensive post-implementation pharmacovigilance study examined adverse event reports from over 130 countries using VigiBase, a global database maintained by the World Health Organization (WHO) [8]. The significance of continuous surveillance of safety is shown by the effect of false information on confidence in medical facilities and vaccination campaigns during the pandemic [9]. Mechanisms like the National Pharmacovigilance System (NPS) are important because they guarantee the safety of the COVID-19 vaccine when it is put on the market [10]. Analyzing adverse events after vaccination (AEFIs) is another crucial way to assess the safety and effectiveness of vaccines across a range of populations [11]. When taken as a whole, these observations highlight how important pharmacovigilance is to reducing risks and promoting public confidence in COVID-19 immunization campaigns around the globe. Pharmacovigilance is crucial in recognizing, monitoring, and avoiding negative drug reactions which pose significant clinical, social, and economic risks. ADRs can lead to life-threatening situations, disrupt effective treatments, and result in prolonged hospitalizations and additional medical interventions [12].

Scope of Pharmacovigilance

Pharmacovigilance (PV) relies heavily on information, which includes gathering, analyzing, and sharing data to ensure patient safety. A strong information system that makes it easier to gather reports of unpleasant events from patients and medical providers, and other stakeholders is the cornerstone of Pharmacovigilance. The development of data sources, with a focus on integrating wearable technology, electronic health records, and empirical evidence to increase the scope and depth of data available for analysis. By automating signal identification and predictive modeling, cutting-edge technologies like artificial intelligence and machine learning are revolutionizing Pharmacovigilance [13]. A normal PV organization involves various stakeholders, organizational units, and functions, as illustrated in Figure 1.

Goals of Pharmacovigilance

Enhance patient well-being and safety through responsible medication use and medical interventions.From laboratory research to long-term post-marketing surveillance, examine the effectiveness of drugs and keep an eye out for adverse responses. Detect and address severe drug-related effects. Protect public health by ensuring safe medication practices. Encourage pharmacovigilance education, training, and awareness while promoting open dialogue with the general population [14]. A Goals of Pharmacovigilance involves various systems and functions as illustrated in Figure 2.

Figure 1: A Normal Pharmacovigilance Organization

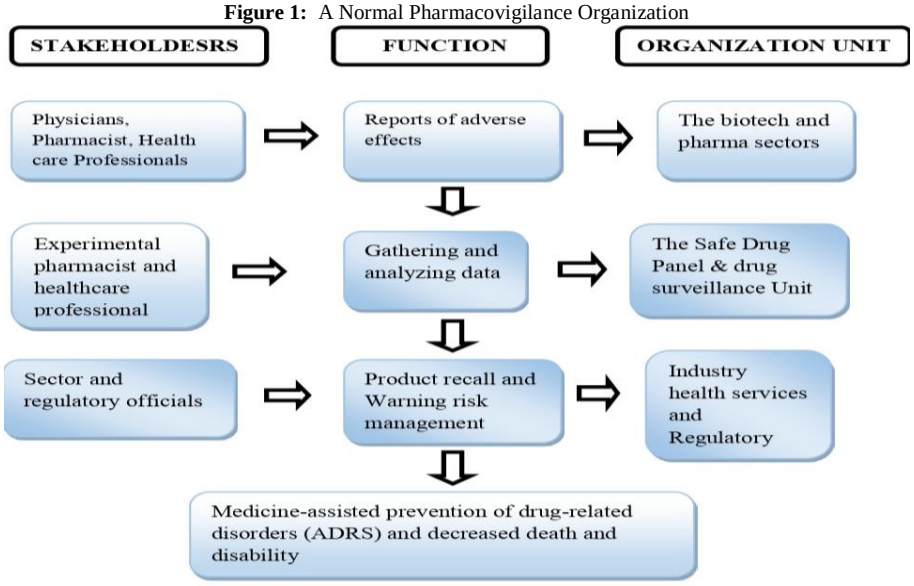
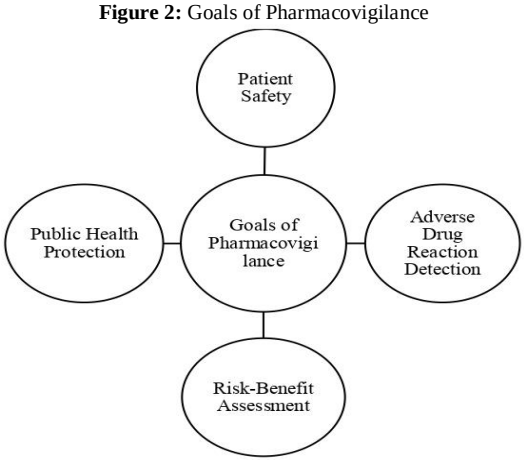


Figure 2: Goals of Pharmacovigilance



Need of Pharmacovigilance

A lot of information on the safety of new pharmaceutical treatments is still unknown when they are first put on the market. For a variety of illnesses, these medications are taken by different patients. The effects of medication may be negatively impacted by these individuals' use of multiple other medications, as well as their adherence to various customs and dietary regimens. Adverse drug responses can also happen when medications are used with herbal and traditional remedies, which need to be closely watched by pharmacovigilance [15]. The necessity of continuous pharmacovigilance is shown by the fact that many side effects, medication interactions, and risk factors have been documented years after a medicine's release, as shown in Table 1 [16, 17].

Table 1: Common Drug Interactions

Types of Drugs	Consequences
Antidiabetic	Reduce glucose level
Warfarin	Higher chance of blood loss
Phenytoin	Breathing problems
Tetracycline	Low tetracycline's absorption
Amino glycoside	Ear and renal issues
Barbiturates	Muscle weakness, Reduced consciousness, coma
Benzodiazepines	Sedation and Respiratory suppression
Lithium	Hypothermia
Alprazolam	Depression of the central nervous system
Miconazole	Severe hypoglycemia
Theophylline's	Insomnia, seizures, restlessness
Ethanol	Additive CNS effect, Death
Methotrexate	Bone marrow suppression

National Pharmacovigilance Centers are Responsible For

Drug safety is closely monitored by National Pharmacovigilance Centers. Among their primary duties are:

Encouraging patients and medical staff to report negative responses.

Gathering or documenting case reports of adverse reactions.

Analyzing and interpreting patterns of adverse reactions.

Identifying potential safety signals amidst background noise.

Recommending regulatory actions based on evidence-driven findings.

What to report

Every alleged negative reaction linked to drugs, including those believed to have been brought on by typical, choice, or medical treatments, should be reported, according to the National Pharmacovigilance Programme (NPP). It would be crucial to report adverse reactions that seem common or inconsequential since they could point to a widespread prescription issue. Any probable side effects of newly approved medications and "Drugs of Current Interest" (as defined by CDSCO) every possible medication interaction adverse medication reactions that have a major influence on patient care, such as: Deathly responses, Prolonged or initial hospitalization, Severe impairment (persistent or permanent), Birth defects

Who can report?

Physicians, dentists, nurses, and pharmacists are among the health care providers who can report suspected adverse drug occurrences. Reports from non-healthcare professionals or members of the general public will not be accepted by the program.

Where can we report?

The completed form must be sent back or returned to the original pharmacovigilance center. Anywhere in the nation can be reported via the pharmacovigilance center that is closest to the reporter. You may find a comprehensive list of pharmacovigilance centers at www.cdsco.nic.in. When in confusion, the Central Drugs Standard Control Organization in New Delhi can receive form which is the national pharmacovigilance center [14].

Physician Responsibility: Drug Safety and Pharmacovigilance

In comparison to patient-specific risk factors including multiple medical condition, advanced age, medication errors, and multiple medication use (polypharmacy) may all be factors linked to the incidence of adverse drug reactions (ADRs) [18]. It can be difficult to identify adverse drug reactions (ADRs) and distinguish them from other illnesses or comorbidities. To do so, practitioners must be knowledgeable about the clinical pharmacology fundamentals of ADRs, such as their kinds, dose-relatedness, allergic reactions, time connections, and risk factors. Suppose that, continuous exposure may be necessary for the development of continued problems such Atypical fractures of the femur caused by bisphosphonates [19]. Recurrence of medical disorders can also result from stopping drugs, such as the elevated risk of bone loss when denosumab is stopped [20]. The various ADR classifications are given in Table 2 [21].

Table 2: Adverse medication reaction classification

Reaction types	An explanation
A: Dose dependent	Exaggerated anticipated side effects from medications taken at regular dosages, such as bleeding when using warfarin or bradycardia when taking beta-blockers
B: Idiosyncratic	Totally unconnected medicinal characteristics, such as allopurinol's ability to treat Steven's Johnson syndrome
C: Dose & time dependent	Associated with long-term cumulative medication use, such as corticosteroid-induced adrenal insufficiency
D: Delayed	Evidently just using medications after a while, such as topical tacrolimus for skin malignancies
E: Withdrawal	As a result of withdrawal or quitting a medicine, such as transient tachycardia when beta-blocker medication are stopped
F: Failure of therapy	linked to unanticipated treatment failure, potentially as a result of a pharmacological interaction (e.g., St. John's Wort decreasing the potency of pill-based contraceptive combinations
G: Genetic	linked to permanent damage to genes, such as phocomelia following thalidomide
H: Hypersensitivity	Linked to a hypersensitive patient's immunological-mediated reaction to medications, like interstitial nephritis (immune complex) and penicillin.

Applying Data Mining and Pharmacogenomics in Pharmacovigilance to Improve Drug Safety

Pharmacogenomics Function in Pharmacovigilance

Pharmacogenomics (PGx) integrates improved understanding of amino acids, DNA, and single nucleotide polymorphisms (SNP) with conventional medicinal sciences like biochemistry. By linking a substance's toxicity or effectiveness with polymorphisms of one nucleotide or the activity of genes, this method addresses how genetic diversity affects a patient's response to a medication. PGx aims to rationally adjust drug therapy in relation to the patient's genotype to obtain the greatest benefit with minimal undesirable effects [22]. With these methods, "personalized medicine" drugs and a bright future lies in medication combinations that are customized to each person's unique genetic makeup. The study of a few uncommon and occasionally coincidental severe reactions (phenotypes) seen in certain people gave rise to the field of pharmacokinetics (PG) [23].

Drug Surveillance using Data Mining

A study of improving the safety and treatment of patients with regard to medication use by collecting, monitoring, analyzing, and assessing data from both patients and medical professionals is known as pharmacovigilance, sometimes called drug safety surveillance. That viewpoint suggests that PV can be divided into two stages, including premarketing examination, which collects information on adverse drug reactions (ADRs) from stages I through III of research studies and preclinical screening and postmarketing surveillance, which gathers data during a drug's postapproval phase and during its entire life on the market [24].

Premarketing monitoring

Pharmacovigilance may be used to predict or assess possible negative drug effects while in the process of producing a medication. Another of the basic techniques for testing compounds utilizing cellular and biochemical assays is experimental in vitro Safe Pharmacological Profile (SPP). The theory states, a compound's influence on a particular target could result in the potential spread of an adverse medication response in persons. Fortunately laboratory screening for ADRs continue to be difficult in respect to both expenditure and effectiveness. [25].

Post-marketing surveillance

The Administration for Food and Drugs (FDA) screens drugs thoroughly before approving them, However, due to the fact that clinical trials are often short, constrained, and skewed by not include individuals with concomitant conditions, It's still possible that a lot of adverse reactions to medications (ADRs) go unreported. It is crucial to maintain postmarket surveillance since real clinical use situations for a range of groups, including inpatients, are not adequately reflected in premarketing trials. PV is crucial in the post-market evaluation of

newly manufactured drugs [26,27]. The competition between pharmaceutical companies and stringent regulatory evaluation procedures promote an elaborate study and creation process before a new drug is brought the society [28].

Spontaneous Reports

Spontaneous reports are voluntary notifications from Physicians or patients to pharmaceutical companies, governing organizations, or different organizations about adverse drug reactions (ADRs) experienced by patients taking medicinal products.

These reports are crucial for identifying potential safety concerns after a drug is approved for market [29, 30].

One crucial method for obtaining safety data for health information for timely identification is the spontaneous reporting of adverse events. It frequently produces safety signals that require additional investigation and is the most likely technique for identifying novel, uncommon ADRs [31].

Cooperation and Alliances

Pharmacovigilance organizations must instead work with other organizations that possess complementary abilities and the capacity to carry out comprehensive drug monitoring and safety investigations. Pharmaceutical quality concerns, such as inferior, spurious, mislabeled, falsified, and counterfeit medicinal products, are being addressed by pharmacovigilance systems more and more [32]. And prescribing error [33]. Although these difficulties have historically been handled by pharmacovigilance mechanisms [34], many of these systems are generally ill-equipped to detect all of these issues, in part because adverse effects aren't first linked to drugs at the point of service. As a second option, many public health organizations may be tasked with looking into a health issue and then determine that it has something to do with medicines [35] did it become clear that recurrence of allergic-like signs and lower blood pressure in patients receiving dialysis treatment in the USA were linked to a specific producer's model of heparin. After the US FDA started collaborating with these organizations, a contaminant was found and the clinical syndrome was further described [36]. Only after the outbreak became widely known did reports of spontaneous adverse events come in, and this encouraged reporting made it challenging to assess the information [37]. The fungus toxicity of the chemical used to administer the epidural was the origin of a fungal meningitis outbreak that local and state health authorities discovered and reported in the United States [38]. Partnerships with specialized public health organizations, such as poison control centers, are therefore crucial. Furthermore, in order to address the pressing public health requirements of an outbreak, pharmacovigilance units in these circumstances must adjust to operating in real time.

CONCLUSION

To ascertain the safety profile of a medication, pharmacovigilance entails a thorough analysis of all relevant data. The advantages of the medication must also be taken into account. Pharmacovigilance remains vital in addressing the challenges arising from the growing diversity and potency of medicines, which inherently pose unpredictable risks. Every medicine entails a balance between therapeutic benefits and potential harm. Minimizing harm necessitates the rational use of high-quality, safe, and effective medicines, coupled with consideration of patient concerns and expectations during treatment planning. By achieving this balance, we can safeguard public health, foster patient trust in their medications, and enhance confidence in healthcare services. This proactive strategy makes it possible to anticipate and manage drug-related problems, informs regulatory revisions, helps the Medical Services and the scientific professions communicate, and informs prescribers about the risks and effectiveness of medications.

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Conflict of Interest

The author declares that they have no conflicts of interest related to this study.

REFERENCES

1. Shivamurthi T, Dixit DC, Ramachandra MS, et al, 2025. Review; Pharmacovigilance and Drug Safety: A Global Perspective. Asian Journal of Pharmaceutical Research and Development. 13(1), Pages 152–160. Doi: https://doi.org/10.22270/ajprd.v13i1.1519.

2. Mansuri A, Uz Zaman T, 2024. Pharmacovigilance: A Necessary Tool for Drug Safety Monitoring Globally. Journal of Drug Delivery and Therapeutics. 14(4), Pages 96–103. Doi: https://doi.org/10.22270/jddt.v14i4.6516.

3. Campbell JE, Gossell-Williams M, Lee MG, 2014. A review of pharmacovigilance. West Indian Medical Journal. 63(7), Page 771. Doi: https://doi.org/10.7727/wimj.2013.251.

4. Beninger P, 2018. Pharmacovigilance: an overview. Clinical Therapeutics. 40(7), Pages 1087–1095. Doi: 10.1016/j.clinthera.2018.07.012.

5. Soni R, Kesari B, 2014. A review on pharmacovigilance. International Journal of Pharmaceutical Sciences Review and Research. 26(2), Pages 237–241.

6. Bihana K, Lebrun-Vignes B, Funck-Brentano C, et al, 2020. Uses of pharmacovigilance databases: an overview. Therapies. 75(4), Pages 355–362. Doi: 10.1016/j.therap.2020.02.022.

7. Kim MS, Jung SY, Ahn JG, et al, 2022. Comparative safety of mRNA COVID-19 vaccines to influenza vaccines: A pharmacovigilance analysis using WHO international database. Journal of Medical Virology. 94(3), Pages 1085–1095. Doi: 10.1002/jmv.27424.

8. Lindquist M. VigiBase, 2008. The WHO global ICSR database system: Basic facts. Drug Information Journal. 42(5) Pages 409–419. Doi: 10.1177/009286150804200501.

9. Rudolph A, Mitchell J, Barrett J, et al, 2022. Global safety monitoring of COVID-19 vaccines: How pharmacovigilance rose to the challenge. Therapeutic Advances in Drug Safety. 13, Pages 20420986221118972. Doi: 10.1177/20420986221118972.

10. Amaro C, Monteiro C, Duarte AP, 2022. COVID-19 vaccines adverse reactions reported to the pharmacovigilance unit of Beira Interior in Portugal. Journal of Clinical Medicine. 11(19), Pages 5591. Doi: 10.3390/jcm11195591.

11. Ferrara F, Mancaniello C, Varriale A, et al, 2022. COVID-19 mRNA vaccines: A retrospective observational pharmacovigilance study. Clinical Drug Investigation. 42(12), Pages 1065–1074. Doi: 10.1007/s40261-022-01216-9.

12. Inácio P, Cavaco A, Airaksinen M, 2017. The value of patient reporting to the pharmacovigilance system: a systematic review. British Journal of Clinical Pharmacology. 83(2), Pages 227–246. DOI: 10.1111/bcp.13098.

13. Bharati A, Dubey T, Thakur R, et al, 2024. A review article of pharmacovigilance and studies of clinical research for health care. IP International Journal of Comprehensive and Advanced Pharmacology. 9(2), Pages 116–124. Doi: 10.18231 /j.ijcaap.2024.017.

14. Alhat BRA, 2011. Pharmacovigilance: an overview. International Journal of Research in Pharmaceutical Chemistry. 1(4), Pages-968–974.

15. S S Shuka, Bina Gidwani, R. Pandey, et al, 2012. Importance of Pharmacovigilace in Indian Pharmaceutical industry. Asian journal of Research in Pharmaceutical Sciences. 2(1), pages 04-08. Doi: 10.52711/2231-5659.

16. Joshi SR, Sapatnekar SM, 2008. Pharmacovigilance in India: how safe are the new drugs? How sure are we? Journal of the Association of Physicians of India. 56, Pages 933-934.

17. Olsson S, 2008. Pharmacovigilance training with focus on India. Indian Journal of Pharmacology. 40, Pages S28-S30. Doi: 10.4103/0253-7613.40241.

18. Rosli N, Teo SP, 2020. Reducing medication error and polypharmacy in older people. Asian Journal of Gerontology and Geriatrics. 15, Pages 86-90. Doi: 10.12809/ajgg-2020-411-ra.

19. Choo SZL, Ahmad MH, Teo SP, 2020. Atypical femoral fracture secondary to long-term bisphosphonate use: a case report. Asian Journal of Gerontology and Geriatrics. 15, Pages 32-33. Doi: 10.12809/ajgg-2019-370-cr.

20. Teo SP, 2020. Denosumab for the treatment of osteoporosis. Aging Pathobiology and Therapeutics. 2, Pages 168-170. Doi:10.31491/APT.2020.09.034

21. Aneesh TP, Sonal Sekhar M, Jose A, et al, 2009. Pharmacogenomics: the right drug to the right person. Journal of Clinical Medicine Research. 1, Pages 191-194. Doi: 10.4021/jocmr2009.08.1255.

22. Brockmöller J, Tzvetkov MV, 2008. Pharmacogenetics: data, concepts and tools to improve drug discovery and drug treatment. European Journal of Clinical Pharmacology. 64, Pages-133-157. Doi: 10.1007/s00228-007-0424-z.

23. Berlin JA, Glasser SC, Ellenberg SS, 2008. Adverse event detection in drug development: recommendations and obligations beyond phase 3. American Journal of Public Health. 98, Pages 1366-1371. Doi: 10.2105/AJPH.2007.124537.

24. Whitebread S, Hamon J, Bojanic D, et al, 2005. Keynote review: in vitro safety pharmacology profiling: an essential tool for successful drug development. Drug Discovery Today. 10, Pages 1421-1433. Doi: 10.1016/S1359-6446(05)03632-9.

25. McClure DL, 2009. Improving drug safety: active surveillance systems should be paramount. Pharmaceutical Medicine. 23, Pages 127-130. Doi: 10.1007/BF03256760.

26. Shibata A, Hauben M, 2011. Pharmacovigilance, signal detection and signal intelligence overview. Proceedings of the 14th International Conference on Information Fusion (FUSION-2011), Chicago, IL, Pages- 1-7.

27. Lopes P, Nunes T, Campos D, et al, 2013. Gathering and exploring scientific knowledge in pharmacovigilance. Public Library of Science ONE. 8(12), Pages e83016. Doi: 10.1371/journal.pone.0083016.

28. Xu L, Anchordoquy T, 2011. Drug delivery trends in clinical trials and translational medicine: challenges and opportunities in the delivery of nucleic acid-based therapeutics. Journal of Pharmaceutical Sciences. 100, Pages 38-52. Doi: 10.1002/jps.22243.

29. Robb MA, Racoosin JA, Sherman RE, et al, 2012. The US Food and Drug Administration's Sentinel Initiative: expanding the horizons of medical product safety. Pharmacoepidemiology and Drug Safety. 21, Pages 9-11. Doi: 10.1002/pds.2311.

30. Waller PC, Evans SJ, 2003. A model for the future conduct of pharmacovigilance. Pharmacoepidemiology and Drug Safety. 12, Pages 17-29. Doi: 10.1002/pds.773.

31. Gostin LO, Buckley GK, Kelley PW, 2013. Stemming the global trade in falsified and substandard medicines. The Journal of the American Medical Association. 309(16), Pages 1693-1694. Doi:10.1001/jama.2013.3048.

32. Bencheikh RS, Benabdallah G, 2009. Medication errors: pharmacovigilance centres in detection and prevention. British Journal of Clinical Pharmacology. 67(6), Pages 687-690. Doi:10.1111/j.1365-2125.2009.03426.x.

33. Aagaard L, Meyer U, Schaefer M, et al, 2012. Pharmaceutical production problems detected by adverse drug reactions reports: a documentary study from the German Democratic Republic, 1982–1990. Clinical Toxicology. 2(120), Pages 2161-0495. Doi:10.4172/2161-0495.1000120.

34. Blossom DB, Kallen AJ, Patel PR, et al, 2008. Outbreak of adverse reactions associated with contaminated heparin. The New England Journal of Medicine. 359(25), Pages 2674-2684. Doi: 10.1056/NEJMoa0806450.

35. Kishimoto TK, Viswanathan K, Ganguly T, et al, 2008. Contaminated heparin associated with adverse clinical events

and activation of the contact system. The New England Journal of Medicine. 358(23), Pages 2457-2467. Doi: 10.1056/NEJMoa0803200.

36. McMahon AW, Pratt RG, Hammad TA, et al, 2010. Description of hypersensitivity adverse events following administration of heparin that was potentially contaminated with over sulfated chondroitin sulfate in early 2008. Pharmacoepidemiology and Drug Safety. 19(9), Pages 921-933. Doi:10.1002/pds.1972.

37. Kainer MA, Reagan DR, Nguyen DB, et al, 2012. Fungal infections associated with contaminated methylprednisolone in Tennessee. The New England Journal of Medicine. 367(23), Pages 2194-2203. Doi: 10.1056/NEJMoa1212972.