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Pharmacovigilance: A Comprehensive Review

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ABSTRACT

Pharmacovigilance is really important for keeping an eye on and assessing Adverse Drug Reactions (ADRs). It's a vital part of how we regulate drugs, practice medicine, and protect public health. As more ADRs are reported, there's a growing need for expert help to spot drug risks and keep products safe. The Uppsala Monitoring Centre heads a global network for pharmacovigilance, and it could be even better with an independent review system to tackle significant drug safety issues that affect people everywhere. While it has mainly focused on finding unexpected or misunderstood side effects in the past, pharmacovigilance is now spreading across the globe and becoming a key part of clinical research. Despite its expansion, this field still faces big hurdles in improving drug safety and monitoring. This review will take a closer look at drug safety, global pharmacovigilance centers, what they do, the benefits and challenges they face, and where healthcare might be headed in the future.

Keywords: Drug safety, Erice declaration, pharmacovigilance, Clinical trials, Drug safety and efficacy, Drug monitoring.

Introduction to Pharmacovigilance

Pharmacovigilance is all about keeping an eye on the effects of drugs, as the WHO puts it. It's a key part of making sure that medications are safe and helps both healthcare providers and patients make better decisions. Even with progress in the field, bad reactions to drugs are still a big issue, leading to sickness and death around the globe.

The word “pharmacovigilance” has roots in Greek and Latin, reflecting its main goal of careful monitoring of drugs throughout their use. With the rise of technology like AI, machine learning, and advanced data analysis, pharmacovigilance has evolved. We can now monitor safety in real time and spot issues more effectively.[1]

Looking ahead, we can expect to see more use of real-world evidence, better teamwork across the globe, and increased reliance on AI to foresee drug reactions. Yet, there are still hurdles to overcome, such as keeping track of drugs sold online, managing complicated treatments like polypharmacy and biologics, and finding a balance between public health needs and the interests of pharmaceutical companies. Moreover, underreporting and insufficient infrastructure in developing nations hinder effective safety monitoring. Tackling these challenges and improving awareness, infrastructure, and global cooperation is essential for boosting pharmacovigilance and safeguarding public health.[2]

Historical Perspectives of Who - Drug Safety Monitoring

Pharmacovigilance began after the thalidomide disaster in the late 1950s and early 1960s.

Thalidomide, which was given for morning sickness, resulted in serious birth defects. This tragic event highlighted the importance of keeping an eye on drug safety even after they are on the market. In 1968, the World Health Organization (WHO) took action by starting the International Drug Monitoring Programme, which marked the beginning of organized global efforts in pharmacovigilance.

(A) Thalidomide Tragedy (1950s–1960s)

The thalidomide tragedy brought to light serious issues with drug safety, particularly for expectant mothers and their babies. It highlighted how important it is to conduct thorough testing before a drug gets the green light and to keep an eye on medications after they hit the shelves. In response, platforms were established for reporting side effects, including those from the WHO and FDA. This unfortunate event also prompted new regulations that require evidence of a drug's safety and effectiveness, fostered international teamwork, and raised the public's call for openness and ethical practices in the way drugs are developed and regulated.[3]

(B) WHO Programme for International Drug Monitoring (1968) Establishment of International Pharmacovigilance

Back in 1968, the World Health Organization began a worldwide effort to keep an eye on drug side effects. This initiative allowed countries to collaborate, establish their own safety centers, and exchange information to catch risks early on.

Uppsala Monitoring Centre (UMC)

The Uppsala Monitoring Centre (UMC) started in Sweden in 1978 as a worldwide hub for drug safety. It operates VigiBase, the biggest database for drug side effects around the globe, and provides support for data analysis, training, and identifying risks everywhere.

Standardization of ADR Reporting

The WHO and UMC worked together to create a more consistent way of reporting adverse drug reactions. They adopted standard formats like Individual Case Safety Reports (ICSRs), ICH E2B(R3) electronic formats, and MedDRA terms. This effort made it easier to work efficiently and identify safety problems around the world.[4]

Encouraging National Systems

WHO assisted nations in building their own drug safety systems. They did this by establishing national centers, offering training, and connecting pharmacovigilance with health departments. WHO also encouraged straightforward reporting methods and engaged the public with tools such as MedWatch in the USA, Yellow Card in the UK, and VigiFlow. As a result, more than 150 countries now have effective systems that work to enhance drug safety worldwide.[5]

Strengthening Drug Regulation and Risk Management

Making drug regulations stronger helps keep medicines safe, effective, and of high quality from the start all the way through their use. Organizations in charge of regulating drugs and systems that watch over drug safety, like the WHO's Programme for International Drug Monitoring, check on how drugs are performing from the development stage to after they are on the market. This ongoing safety check is important since clinical trials might not catch rare or long-lasting side effects. Regulatory groups ask pharmaceutical companies to provide documents like Risk Management Plans and Periodic Safety Update Reports to help identify and manage risks. Databases such as VigiBase, run by the Uppsala Monitoring Centre, allow for the worldwide sharing of reports about negative drug reactions. Agencies like the FDA and EMA work to make sure that drugs are safe and meet quality standards, and they fight against poor-quality or fake products through inspections and enforcement. Efforts to harmonize regulations globally, led by the International Council for Harmonisation, aim to bring consistency to regulatory standards.[6]

Promoting a Culture of Drug Safety

Creating a strong culture around drug safety includes everyone: regulators, healthcare workers, pharmaceutical companies, and the public. It all starts with education and awareness. Healthcare providers should have training on how to monitor medications and prescribe them safely, and the public should know how to spot and report adverse drug reactions (ADRs).We need to make it easier for people to report ADRs. This can be done through user-friendly systems like mobile apps or online forms. Linking pharmacovigilance with electronic health records (EHRs) can help with monitoring in real-time. Transparency from organizations like the WHO, FDA, and EMA is essential to build trust by keeping everyone in the loop. Encouraging patients and healthcare providers to make decisions together ensures that treatment options focus on the patient and keep risks in mind. A strong safety culture requires ongoing change, awareness, and teamwork to support public health and maintain trust in our healthcare systems.[7]

(C) FDA and AERS (1970s)

Back in the 1970s, the FDA set up the Adverse Event Reporting System (AERS) because of growing worries about safety, especially after the Thalidomide incident. This system made it possible for doctors, patients, and drug companies to report any bad reactions they saw. This meant the FDA could spot safety issues and react to them much faster. AERS also made information more open and available, giving power to both healthcare workers and patients. By encouraging teamwork among different groups, it improved how safety reports were made. This system was really important for setting up today's FDA Adverse Event Reporting System (FAERS), which uses modern technology to keep an eye on drug safety in real time. AERS played an important role in strengthening drug safety practices by providing a clear, organized way to monitor and assess medications continuously.

(D) ICH Guidelines (1990s)

Back in the 1990s, the International Conference on Harmonisation (ICH) came together with a big goal: to make drug safety and regulations more consistent across Europe, the US, and Japan. One of their key guidelines, E2B, set a standard for how to report adverse drug reactions (ADRs), which helped improve communication and safety checks worldwide. The ICH also encouraged the use of risk management plans, better monitoring after drugs hit the market, and making pharmacovigilance a key part of drug development. This teamwork aimed to ease the regulatory process and boost safety globally. [8]

(E) EU Pharmacovigilance System (2005)

In 2005, the EU put in place a strong system for monitoring the safety of medicines, which is guided by Regulation (EC) No 726/2004 and Directive 2001/83/EC. The European Medicines Agency (EMA) plays a key role in coordinating this effort, while EudraVigilance serves as a central database for collecting and analyzing information about adverse drug reactions (ADRs). Some important aspects of this system are:

- Marketing authorization holders (MAHs) must report ADRs.
- Risk Management Plans (RMPs) are created.
- The Pharmacovigilance Risk Assessment Committee (PRAC) oversees the process.

This system helps ensure quick safety evaluations, regulatory responses, and promotes transparency and collaboration among EU member states.

(F) Periodic Safety Update Reports (PSURs)

Periodic Safety Update Reports (PSURs) represent an essential component of pharmacovigilance, as they are systematically submitted by Marketing Authorization Holders (MAHs) to evaluate the benefit-risk ratio of a pharmaceutical product throughout its commercial lifespan. These reports encompass several critical elements, including:

- Summaries of Adverse Drug Reactions (ADRs)
- Analytical assessments of trends in safety data
- Current evaluations regarding benefit-risk considerations

The implementation of PSURs facilitates the prompt recognition of safety signals, which may subsequently inform regulatory actions such as amendments to product labels or the withdrawal of medications from the market. Initial submissions of these reports typically occur at intervals of six to twelve months; however, this frequency may be adjusted to a lesser timeline, contingent upon the emergence of new safety risks.

The advancement of regulatory standards, exemplified by the International Council for

Harmonisation's E2C (R2) guidelines, has transformed the PSUR framework into Periodic Benefit-Risk Evaluation Reports (PBRERs). This evolution underscores a shift in focus from mere ADR documentation to a more nuanced evaluation of the overall benefit-risk balance associated with pharmaceutical use. Failure to comply with these reporting requirements may lead to punitive actions or the imposition of additional surveillance measures.[9]

Data Sources for PSURs

Periodic Safety Update Reports (PSURs) serve as a mechanism for the aggregation and evaluation of safety data from a variety of sources to assess the ongoing safety profile of pharmaceuticals post-market authorization. These sources encompass reports submitted by healthcare professionals, patients, and pharmaceutical companies, which are collected through established surveillance systems including VigiBase, the FDA Adverse Event Reporting System (FAERS), and EudraVigilance. In addition to these reports, data derived from clinical trials and observational studies, along with relevant medical literature and public health statistics, contribute to the overall safety assessment. Furthermore, documentation maintained by companies and advanced digital systems, such as electronic health records (EHRs) and artificial intelligence tools, facilitate the prompt identification of safety concerns. This multi-faceted approach ensures a thorough and timely evaluation of drug safety in the post-marketing phase.[10]

Contents of a PSUR

A Periodic Safety Update Report (PSUR) serves as a comprehensive document that systematically evaluates the safety profile of a pharmaceutical product. This report encompasses fundamental product information, a thorough summary of all adverse effects reported, an analysis of newly identified safety issues, and an assessment of whether the therapeutic advantages of the drug continue to surpass its associated risks. Additionally, the report addresses the impact of the medication on specific populations, such as elderly individuals and pregnant women, while also examining concerns related to misuse, medication errors, and interactions with other pharmaceuticals.

Submission Timelines

The frequency of submitting PSURs varies based on how long a drug has been on the market. For the first two years after approval, reports are sent in every six months. Then, for the next three years, they’re submitted once a year. If there are no significant safety concerns, the reports are needed every

five years after that. If necessary, authorities can request additional reports. There's also a newer version called PBRER that emphasizes looking at the benefits of the drug compared to its risks.

Transition to PBRERs

Switching from PSURs to PBRERs has made drug safety reporting better by looking at both the good and the bad. PBRERs give a fuller picture by showing how effective the drug is, how it's actually used by people, and how it stacks up against other options. They meet international guidelines, allowing one report to be useful for different regulators, and they help speed up actions like changing warnings or lowering risks.[11]

Digital Era & Signal Detection (21st Century)

Digital tools have made a big difference in spotting drug safety problems. With the help of big data and AI, we can quickly identify safety signals from various sources like health records, pharmacy data, wearable devices, and social media. Technologies like machine learning and natural language processing (NLP) simplify the analysis of unstructured data. Global databases, such as VigiBase, FAERS, and EudraVigilance, enable countries to collaborate and track information together. The real-time monitoring during the COVID-19 vaccine rollout is a good example of how effective these tools can be. Patients also play a part by reporting side effects through apps and online platforms, which makes the system more accessible for everyone.[12]

Benefits of the Digital Era in Pharmacovigilance

Thanks to progress in digital technology, drug safety monitoring has shifted from being done by hand to using automated systems that work in real-time. Tools like AI and machine learning help sift through lots of data to spot trends, while natural language processing catches early warning signs from research articles and talks with patients.

Integration of Big Data Analytics

Big data helps spot harmful reactions to medications and interactions in large groups of people sooner. It also promotes teamwork around the world with shared safety databases and bolsters monitoring of drugs after they hit the market by using real-life evidence. Still, there are some hurdles to overcome, such as protecting people's privacy, making systems work together, and getting everyone on the same page with the information. **Artificial Intelligence (AI) and Machine Learning (ML) in Signal Detection** AI and ML have changed the game in pharmacovigilance when it comes to spotting signals. They allow for fast, automated analysis of huge, varied datasets from places like electronic health records, clinical trials, social media, and wearable tech. These technologies can find patterns and predict bad drug reactions much faster and more accurately than the older ways. A big part of this is Natural Language Processing, which pulls useful information from unstructured data such as medical reports and online feedback from patients. AI also helps figure out safety issues by looking at past data and demographics to assess how likely it is that a safety signal is real. With predictive analytics, we can manage risks better by spotting groups at risk before problems become widespread. Agencies like the FDA and EMA are using AI tools to improve signal detection. Still, there are hurdles to overcome, like data bias, the complexity of AI models, and changing rules in the industry.[13]

Globalization of Pharmacovigilance Databases

The worldwide connection of pharmacovigilance databases has made monitoring drug safety across countries much better. Systems such as WHO's VigiBase, EMA's EudraVigilance, and the FDA's FAERS allow for the real-time exchange of adverse drug reaction (ADR) data, no matter where it comes from. By combining information from around the globe, these platforms help find rare or local ADRs. Thanks to technologies like AI, big data, and automated data mining, the way these international databases work together has become easier and more efficient. However, there are still problems to tackle, like different reporting standards, concerns about data privacy, and varying regulations, which make it tough to achieve full harmony. International organizations are actively working to create standard practices and improve data sharing to keep drug safety a priority worldwide.

Rise of Patient-Centered Pharmacovigilance

Patients are now playing a bigger role in reporting adverse drug reactions (ADRs) thanks to digital health tools and a focus on real-world evidence. With the help of online platforms and mobile apps, patients can easily submit their reports, which helps create a wider and more complete picture of safety data. Social media and patient forums are also great sources for understanding drug safety, and researchers can analyze this information using AI and natural language processing. Data from wearables and electronic health records provide a fuller view of ADRs compared to traditional clinical trials. This change highlights the importance of being open, communicating risks, and making shared decisions between patients and healthcare providers. While there are challenges, such as differences in patient data and the need to ensure it fits with current systems, this new approach is becoming a key part of pharmacovigilance today.

Objectives of Pharmacovigilance

Pharmacovigilance is really important for keeping drugs safe. It keeps an eye on bad reactions to medications, both while they are being tested and after they are available to the public. This process looks at how a drug's advantages stack up against its risks by gathering and reviewing information from different places, such as clinical studies, doctors, and patients. When risks are detected, actions like changing product labels, creating risk management plans, or running more studies are put into place to lessen any harm. It also works to ensure that medications are used safely by providing education and

clear safety messages, and makes sure that any safety updates reach healthcare providers and the public quickly. Following the rules from organizations like the FDA and EMA is essential to stay compliant, and monitoring continues even after a drug hits the market to check for any long-term effects.[14]

Worldwide Soldiers of Pharmacovigilance

Pharmacovigilance brings together people from all over the world to work as a team for drug safety. Every group contributes in its own way to watch for and handle any negative effects from medications, creating a united safety network.**A. Quality Assurance and**

Safety (WHO)

The WHO is at the forefront of worldwide efforts to keep medicines safe. Their goal is to make sure that essential medications are both safe and affordable, and that they are used properly, especially in places that don't have enough resources. The WHO also establishes global standards and encourages teamwork to enhance the safety of medicines around the globe.

B. The Uppsala Monitoring Centre (UMC)

Acts as the main hub for handling ADR reports from various nations.

Ensures that ADR reporting is uniform and standard across the globe.

Aids in spotting safety concerns early and encourages communication on a global scale.

C. National Pharmacovigilance Centers

- These are found in places like hospitals, medical schools, or poison control centers, not only in regulatory bodies.
- They raise public awareness and keep a close eye on drug safety using methods such as Prescription Event Monitoring (PEM).
- Countries such as the UK, US, Sweden, and New Zealand are at the forefront of active monitoring.
- The benefits often outweigh the expenses related to drug harm.[15]

D. Hospitals and Academia

- In hospitals, they keep an eye on patients all the time to catch any drug reactions quickly.
- Universities focus on studying drug safety, teaching professionals, and creating guidelines to ensure safe practices.
- They are important members of ethics boards that help maintain honesty in research and protect patients.

E. Health Professionals

- At first, the focus was just on doctors, but it now extends to include pharmacists, nurses, and other health workers.
- These individuals bring different perspectives and help make ADR reporting more effective.
- A broader approach leads to richer and more precise information about drug safety. **F. Patients**
- Patients share their own stories about medications, which helps with safety understanding.
- The involvement of patients makes the systems that monitor drug safety stronger. • Encouraging patients to report side effects results in better and more informed safety evaluations.[16]

Pharmacovigilance and International Health

Pharmacovigilance plays a vital role in keeping medications safe around the world, and the Uppsala Monitoring Centre (UMC) helps track reports of bad reactions to drugs from different countries. To tackle safety issues related to medications that affect people globally, it is important to improve this system, especially by conducting independent reviews.

UMC and Global Coordination

UMC helps make ADR reporting consistent and encourages cooperation worldwide. This allows for faster identification of safety issues and promotes a collective global approach to managing medication risks.

The Erice Declaration

This is an important document that supports fair, open, and cooperative drug safety monitoring. Good pharmacovigilance depends on clear communication about the risks of medications, where all parties are accountable for providing correct information. It fosters collaboration by encouraging the sharing of data and knowledge, and it invites the public to take part in decisions about safety.

Challenges:

In pharmacovigilance, there are a few key issues. One big problem is the mixed messages that can leave the public feeling confused and less trusting. Also, when there is not enough transparency, it creates doubt among people. Sometimes, national authorities do not work well together, which can slow down responses when health emergencies happen. In certain areas, cultural and economic obstacles make it hard for people to be aware of drug safety initiatives, and centers that lack funding may find it difficult to meet global standards.[17]

The Burden of ADRs

ADRs remain a serious concern for both public health and the economy, leading to sickness, hospitalizations, and higher healthcare expenses. By improving how we monitor these reactions, we can help reduce these problems.

Socio-Political, Economic, and Cultural Factors

The way people think about and use medicines is shaped by their culture, the economy, and the healthcare system in their country. In some places, people really like injectable medications, while in others, advertisements for drugs can be seen directly by consumers. More and more individuals are choosing to self-medicate and purchase medications online. To make sure everyone uses medicines safely, it's important to educate the public about medication safety, reaching every segment of society.

National Pharmacovigilance Centers

These centers play an important role in the WHO's program for monitoring medications. They handle local data on adverse drug reactions, evaluate risks, and provide training for healthcare professionals. Ideally, every country should have a center to help promote national health.

International Response to Drug Safety

Global cooperation is critical due to the cross-border nature of drug safety issues.

Need for Cohesive International Response

Coordinated international assessments are vital, especially during health emergencies like pandemics.[18]

WHO's Role

WHO works to keep drugs safe around the world by teaming up with experts who look over safety information and recommend steps to take. They assist countries with limited resources and offer training and tools for tracking safety. Additionally, WHO collaborates with global centers to make data sharing better. By joining forces in this way, they can quickly address safety issues, maintain consistency, share effective practices, and build public trust in healthcare.

Constituted Pharmacovigilance Program of India

India's Pharmacovigilance Program (PvPI) is a national effort managed by the Central Drugs Standard Control Organization (CDSCO). Its main goal is to keep people safe by tracking any bad reactions to medications. This program is based on the Drugs and Cosmetics Act from 1940 and the rules established in 1945.

Regulatory Framework

In India, the system for monitoring drug safety is supported by the Drugs and Cosmetics Act and is managed by the CDSCO. The National Coordinating Centre (NCC) handles the reporting of adverse drug reactions (ADRs) throughout the nation. It is important for healthcare professionals and pharmaceutical companies to report any negative effects of drugs. The PvPI also aligns with worldwide safety practices, and those who fail to comply may face consequences. The system is updated often to ensure better drug safety.

Key Objectives

Pharmacovigilance aims to keep an eye on bad reactions to medications to identify safety problems. It also focuses on making patient care safer by managing risks, updating everyone involved about safety, educating healthcare workers, and promoting teamwork around the world when it comes to drug safety.[19]

National Coordinating Centre (NCC)

The National Coordinating Centre (NCC) is the main place for all things related to PvPI. It collects and reviews reports on adverse drug reactions (ADRs), communicates safety information to those who need to know, collaborates with Adverse Drug Reaction Monitoring Centres (AMCs), and provides training to improve how ADRs are reported.

Regional Adverse Drug Reaction Monitoring Centres (AMCs)

Adverse Drug Reaction Monitoring Centres (AMCs) serve as local centers for gathering and reviewing reports of drug reactions. They collect details from the community and healthcare workers, send these reports to the National Coordination Center (NCC), and share important safety information. They also offer training and work closely with the NCC to ensure that practices are similar across the country.

Accessible Rporting Mechanism

The CDSCO created an easy-to-use online platform for people to report adverse drug reactions (ADRs). You can submit reports online, by phone, or through written notes. This system is open to healthcare workers and anyone from the public. There are also educational initiatives to raise awareness, while AMCs and the NCC work on managing and looking into the reports effectively.[20]

CONCLUSION

Pharmacovigilance plays an important role in addressing the challenges that come with the growing variety and strength of medications, which can sometimes lead to unexpected harm. When side effects and toxicity occur, especially if they are new, it's vital to report and examine them, and then share this information clearly with those who can understand it. Every medication comes with a balance between its benefits and the risk of harm. We can reduce the risk by using safe, effective medicines wisely and by considering patients' concerns and expectations when making treatment choices.

Reference

1.Coleman JJ, Pontefract SK. Adverse drug reactions. Clin Med (Lond). 2016;16:481–41. Collamati A, Martone AM, Poscia A, Brandi V, Celi M, Marzetti E, Cherubini A, Landi F. Anticholinergic drugs and negative outcomes in the older population: from biological plausibility to clinical evidence. Aging Clin Exp Res. 2016;28:25–35.

2.Dean L. Clozapine therapy and CYP2D6, CYP1A2, and CYP3A4 genotypes. In: Pratt V, McLeod H, Rubinstein W, Dean L, Kattman B, Malheiro A, editors. Medical genetics summaries. Bethesda: National Center for Biotechnology Information (US); 2012.

3.Fornasier G, Francescon S, Leone R, Baldo P. An historical overview over pharmacovigilance. Int J Clin Pharm. 2018;40:744–7.

4.Gaitatzis A, Sander JW. The long-term safety of antiepileptic drugs. CNS Drugs. 2013;27:435–55.

5.Garon SL, Pavlos RK, White KD, Brown NJ, Stone CA Jr, Phillips EJ. Pharmacogenomics of off-target adverse drug reactions. Br J Clin Pharmacol. 2017;83:1896–911.

6.Gentry CA, Rodvold KA. How important is therapeutic drug monitoring in the prediction and avoidance of adverse reactions? Drug Saf. 1995;12:359–63.

7.Gerlach M, Egberts K, Dang SY, Plener P, Taurines R, Mehler-Wex C, Romanos M. Therapeutic drug monitoring as a measure of proactive pharmacovigilance in child and adolescent psychiatry. Expert Opin Drug Saf. 2016;15:1477–82.

8.Guerrini R, Perucca E. Genetic testing to prevent adverse reactions to antiepileptic drugs: Primum non nocere. Neurology. 2018;90:155–6.

9.Hadi MA, Neoh CF, Zin RM, Elrggal ME, Cheema E. Pharmacovigilance: pharmacists' perspective on spontaneous adverse drug reaction reporting. Int Pharm Res Pract. 2017;6:91–8.

10. Haen E. Therapeutic drug monitoring in pharmacovigilance and pharmacotherapy safety. Pharmacopsychiatry. 2011;44:254–8.

11. Harmark L, van Grootheest AC. Pharmacovigilance: methods, recent developments and future perspectives. Eur J Clin Pharmacol. 2008;64:743–52.

12. Hiemke C, Bergemann N, Clement HW, Conca A, Deckert J, Domschke K, Eckermann G, Egberts K, Gerlach M, Greiner

13. DK Tripathi S Shiv Pharmacovigilance (Nirali Prakashan)2017262

14. R Dr history And Development of pharmacovigilance110

15. S Nimesh Pharmacovigilance program of review article Acta scientific pharmaceutical sciences2022

16. RK Sahu R Yadav Adverse drug reaction monitoring prospects and impending challenges for pharmacovigilance

17. MR Sutar DR Gawne Review article of study of drug regulatory approval process and comparative requirement of common technical document in Europe,USA and India in coordination with drug development processInt J Pharm Sci20132026879

18. Y Sachdev Pharmacovigilance safety matter, Indian pharmacology2008

19. AK Mohiuddin Department Of pharmacy, world University of Bangladesh, green road, Dhaka , Bangladesh

20. S Caffrey C Paul Generic drugs – The Indian scenarioJ Postgrad Med2019652679