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PHARMACOVIGILANCE: THE CORNERSTONE OF DRUG SAFETY AND PUBLIC HEALTH

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ABSRTACT

Pharmacovigilance is a crucial aspect of drug development and post marketing surveillance ,ensuring the safety and efficacy of medications .This review article highlights the significance of pharmacovigilance in identifying and mitigating adverse drug reaction (ADRs),optimizing drug therapy, and enhancing patient outcomes .we discuss the importance of signal detection, strengthening ,and validation in pharmacovigilance ,and explore the role of advanced technologies and data analytics in enhancing drug safety monitoring .Additionally,we examine the challenges and opportunities in pharmacovigilance ,including the need of robust regulatory frameworks, effective communication strategies, and international collaboration .By emphasizing the critical role of pharmacovigilance in safeguarding public health,this review aims to promote a culture of vigilance and continuous improvement in drug safety monitoring.

Keywords: Pharmacovigilance, Drug Safety, Adverse Drug Reactions, Signal Detection, Public Health.

I. INTRODUCTION

The science and activities relating to the detection, assessment ,understanding and prevention of adverse effect or any other possible drug-related drawback ,particularly ,long-term and short -term adverse effects of medicines ,is how World Health Organization define pharmacovigilance . [5] Pharmacovigilance commonly referred to as post marketing surveillance , is another name of phase 4 of the drug development of process [13] Pharmacovigilance has the significant and essential role in clinical research[4] The term pharmacovigilance have their roots in Greek word pharmacon ,which means drug and latin verb vigilare which means to keep watch [6] When selecting a medication for therapy, it is essential to make sure that both the patient and the doctor have access to sufficient information [1] Even so research shows that there are still significant adverse drug reactions to medications, which are a prevalent but frequently avoidable source of disease, disability, and even death [2] Every medication has the potential to have negative side effects, so there is always a risk involved. When determining whether or not to employ a specific medication in a given patient, the level of risk must be taken into account in addition to the projected therapeutic benefit.[19] Adverse drug reaction (ADRs) account for 6.55 to 6.89% of all hospital pyadmissions. These events lengthen hospital stays and increase patient expenses. [20,21] More than 50% of ADRs are unquestionably or maybe avoidable, according to Patelet et al's 2007 research.[22] These adverse drug reactions (ADRs) put a financial strain on society in addition to making patients' suffering worse and raising rates of morbidity and mortality.6.7% (0.1-0.85%) is the estimated total incidence of ADRs among hospitalized patients.[7] According to data, deaths from ADRs are 19.18% higher and hospital stays are 8.25% longer in patients who are World Health Organization experienced. The average increase in medical costs for patients with ADRs was 19.86% [8] Pharmacovigilance's most crucial component is signal detection and assessment [23] Particular signal, according to the World Health Organization is "reported information on a possible causal relationship between an adverse event and a drug, of which the relationship is unknown or incompletely documented previously ." A small number of reports frequently indicate something [24]

History of Pharmacovigilance :

Global initiatives were sparked by the thalidomide catastrophe of the 1960s, which was a turning point in drug safety. Concerns were further stoked by the 1893 Lancet article on chloroform deaths. Following thalidomide and succinylamide elixir deaths, respectively, the US FDA Act was amended in 1906 and 1962 to address safety concerns. The World Health Organizations's Program for international Drug Monitoring in 1968 and the UK's Medicines Act of 1968 both contributed to the globalization of drug safety initiatives. [35,36]

The Development of sequential pharmacovigilance ; [35,36]

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Table no: 1

Year	Development
1747	Very first known clinical trials by James Lind, proving the usefulness of lemon juice in preventing scurvy.
1937	Death of more than 100 children due to toxicity of sulfanilamide
1950	Apalstic anemia reported due to chloramphenicol toxicity
1961	Worldwide tragedy due to thalidomide toxicity
1963	16th world health congregation recognize significant to rapid action on adverse Drug Reactions (ADRs).
1968	Who research project for international drug monitoring on pilot scale .
1996	Global standards level clinical trials initiated in india.
1997	India attached with WHO Adverse Drug Reaction Monitoring Program.
1998	Initiation of pharmacovigilance in India.
2002	67th National Pharmacovigilance Center established in India.
2004-05	India launched National Pharmacovigilance Program.
2005	Accomplishment of structured clinical trials in India.
2009-10	Pharmacovigilance Program (PvPI) started.

FUNDANMENTALS OF PHARMACOVIGILANCE ;

A key component of public health policy is pharmacoviligance, which is concerned with identifying, evaluating, and averting hazardous drug reactions. ADRs cost the EU $80 billion a year in hospital admissions (5%of all hospital admissions) and 200,000 deaths. The WHO's worldwide drug monitoring program, which was started in 1968 with ten countries, is currently overseen by over 100 and maintains a database with 10 million reports of adverse reactions.[37]

ADVERSE DRUG REACTIONS:

Even when prescribed drugs are used as directed, patients may experience adverse drug reactions (ADRs) from time to time. A side effect is not the same as an adverse pharmacological reaction. In the area of pharmacovigilance, the assessment of ADRs is especially important. [40] In contrast to toxic or side effects adverse effects cover all unintended pharmacological side effects and do not assume a mechanism. The quality of life of patients is impacted by unanticipated and negative outcomes during clinical use, known as adverse drug reactions (ADRs). 10% -20% of hospitalized patients experience adverse drug reactions (ADRs) which account for 5% of hospital admissions. Mitigating injury requires prompt detection and management.[38]

CLASSIFICATION OF ADR:

At first there were two types of adverse drug reactions (ADRs): Type A (does-dependent,predictable) and Type B (unpredictable) .Types C (chronic) and D (delayed) were added afterwards. Type E withdrawal and Type F therapeutic failure ensued. Hospital ADRs are categorized as Type A, which are frequently avoidable. In adults, common offenders include corticosteroids, antibiotics, and cardiovascular medications; in children, common offenders include anti-Infectives, respiratory medications, and vaccinations. Go to DRUG SAFETY for comprehensive management strategies.[38]

PREDICTABLE (TYPEA) REACTION:

The medicines's pharmacologic features, such as an enhanced yet measurable response to the drug that includes aspect effects, gyanogenic effects, and withdrawal symptoms, were supported by these. [9,10]

UNPREDICTABLE (TYPE B) REACTION:

These square measurements, which take into account the patient's unique characteristics rather than the recognized effects of the medication, represent allergy and specialization. These occur less frequently,are

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usually not dose-related, are usually rather serious, and need drug withdrawal. A list of some suspected and confirmed medications with negative effects. [9,11,10]

Below lists the known drug and its side effects.[12]

Table No 2

Drug	Adverse Drug Reaction
Thalidomide	Phocomelia, Multiple defects
Methotraxate	Multipal defects, Foetal death
Androgen	Virilization, limb, esophageal, cardiac defects
Progestins	Virilization of female foetus
Stilboestrol	Vaginal carcinoma in teenage female offsprings
Tetracyclines	Discolored or deformed teeth, retarted bone growth
Warfarin	Nose, eye and hand defects ,growth retardation
Phenytoin	Various malformations
Lithium	Foetal goiter ,cardiac and other abnormalities
Aspirin/Indomethacin	Premature closer of ductus arteriosus

ASSESSMENT OF ADR:

1) Continued advancement of automatic signal detection programs that are utilized in programs of spontaneous monitoring.
2) Enhancement in evaluating medication safety issues with global significance.
3) Encourage cooperative ties between nations on a local and global scale so that nations can evaluate drug safety crises and react accordingly.
4) Think about ways to include local drug usage patterns into pharmacovigilance data when evaluating the benefits and risks at the federal level.[39]

POST MARKETING SAFETY DRUG MONITORING:

Drug interactions can be found, the environmental impact of medications used in large population can be calculated, the contribution of "inactive" ingredients to the safety profile can be evaluated, systems for comparing the safety profiles of similar medications can be used, and the negative health effects of drug residues in animals-such as antibiotics and hormones-can be monitored. A more methodical way to evaluating the value of currently accessible medications has been made possible by the Council for International Organization of Medical Science (CIOMS)study on benefit –RISK assessment of drugs after marketing[3].In order to prevent significant advancements from being lost in an overly tight regulatory web, it is now widely acknowledged that a portion of the process of accessing drug safety must take place in the post –marketing (approval) phase. The regulators will make the decision about whether and how this might occur. [39] In the regulatory context, spontaneous reporting is still essential for pharmacovigilance and signal detection, but there is also growing evidence that more active surveillance is required. The frequency of an ADR related to a product or its safety in comparison to a comparator cannot be ascertained from spontaneous reports without information on usage and consumption levels.[39]

SIGNAL:

Information that has been reported about a potential link between a medication side effect and an adverse event, either not fully understood or with insufficient prior documentation. Generally, depending on the severity of the incident and the accuracy of the information, multiple reports are needed to produce a signal. An evaluation or other action is typically required when a signal is published.[14]

SUBCATEGORIES OF SIGNAL:

(1) Regulatory signal: These signs include one or more severe adverse events, unanticipated adverse events, changes in the frequency or kind of anticipated adverse drug reactions, changes in the severity of existing adverse drug reaction, and more.

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(2) Intermediate signal: If a signal is built up and no determination is made regarding whether it is closed or validated afterwards
(3) Verified signal: When a fresh signal emerges, it represents a genuine or authentic risk.
(4) Refuted signal: Once work-up was completed, a false and closed signal was generated, with no risk or potential risk.
(5) New Signal : A signal that is recognized and detected right now.
(6) On Going Signal: A signal under examination, tracking, and work-up that has been assessed for some time.
(7) Closed Signal: After every step of the signal detection process, a signal that has been assessed and recorded.[15]

SIGNAL DETECTION:

The pharmaceutical business ,regulators, and the general public re all very interested in the early detection of safety signals.

[25] Both qualitative and quantitative elements are present in signals. Various adverse event categories require distinct detection techniques. Pharmacovigilance primary goal is early signal detection . [26] Late signal detection caused the thalidomide disaster of the 1960s. [27] There are numerous ways to produce a signal, including: (15]

1. Spontaneous reporting
2. Prescription event monitoring
3. Registries
4. periodic safety Update Report (PSUR)
5. Signal generation by trigger tools
6. Case control studies
7. Cohort studies

1) SPONTANEOUS REPORTING:

The spontaneous reporting system (SRS) is the main foundation of current pharmacovigilance. Most people regard case reports and case series to be a component of the spontaneous reporting system. Finding type B effects and peculiar type A effects is much easier with its assistance.The primary purpose of SRS is to identify novel, uncommon, and dangerous ADRs early on by signal detection. An individual with the necessary medical qualifications reports spontaneously to a pharmacovigilance centre, where the reports analyzed [28,29]

2) PRESCRIPTION EVENT MONITORING :

Prescription Event Monitoring is a method used to keep track of all patients who have been given specific medications .These type of proactive monitoring was created in the UK (Prescription Event Monitoring)and New Zealand (Intensive Medication Monitoring Program).[30,31]

3) REGISTRIES:

Disease and drug registries are both able to produce sufficient safety signals. A registry is essential a group of patients who have similar clinical presentations. Disease (disease registries)and specific exposure (drug registries)are examples of characteristics .[32]

4) PERIODIC SAFETY UPDATE REPORT :

When looking for new safety signals, the PSUR might be a valuable resource. A PSURE is meant to give the Competent Authorities an update on the global safety experience ni of a pharmaceutical product at specific intervals after authorization. [33]

5) SIGNAL GENERATING BY TRIGGER TOOL:

Healthcare professionals develop an accurate and dependable approach to identify and measure adverse drug reactions in hospitalized patients. The clinical pharmacist is essential in the early detection of adverse drug reactions (ADRs) and other drug related issues. They also monitor the efficacy of medicines through the use of electronic systems, such as information components (IC) proportional relative risk (PRR), etc.[16]

6) CASE CONTROL STUDIES:

In case control studies, an individual, medication, illness, or outcome is studied retrospectively, descriptively, and through observation.[16]

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7) COHORT STUDIES:

Cohort studies carry out the observational, prospective investigations. This study does the initial updates of the adverse effects and any new adverse event. [16]

SIGNAL STRENGTHING:

Once the basic analysis of the relevant data is complete, a single report is adequate to reinforce the Signal. When qualitative computations are used in data analysis to determine the relative risk, the greater the relative risk, the stronger the signal. A signal is a moment in time captured during the drawn –out process of monitoring an adverse medication reaction. A signal in the market needs to be tracked for a considerable amount of time after it has been verified and evaluated. [17]

SIGNAL MANAGEMENT:

Signal management is frequently explained as a sequential process (as illustrated in figure1) that includes the following steps: detection, validation, confirmation, analysis and prioritization, assessment, and action recommendation.[18]

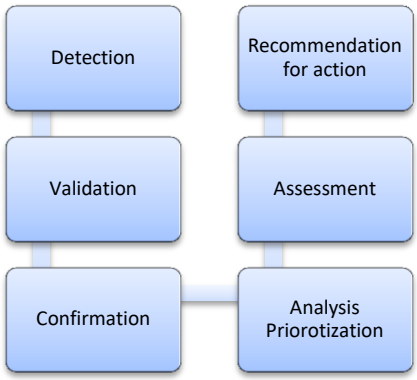

FIG NO: 1

A new potentially causal association, or a new aspect of a known association between an intervention and an event or set of related events, either beneficial or detrimental, that is deemed to be of sufficient likelihood to justify verificatory action, is what signal detection, the first step, looks for in safety data.[41] Validating signals is the second phase in the signal management process. This phase involves evaluating the detected signal to see if there is enough data to support more investigation. [42] In the third phase, The process of signal confirmation identifies the signals that will be covered in the upcoming PRAC conference. [43,44] In the fourth step, known as prioritization, the signals are ranked according to the strength of the evidence, possible impact on public health, and effect on patient health. High priority refers to something that requires immediate attention and handling. [43] In the fifth phase, known as signal assessment, all available scientific evidence about the signal is evaluated. [42]

II. SIGNAL DETECTION METHODOLOGIES

Spontaneous Reporting System:

Pjharmacovigilance signal detection relies heavily on spontaneous reporting systems (SRS).Health care providers and patients submit individual case reports of adverse events to these platforms.SRS is mostly used to find novel, uncommon ,or severe adverse events that went unnoticed in clinical studies. The process of detecting signals may be impacted by spontaneous reports 'occasional inclusion of erroneous or incomplete data.[34]

Data Mining Technique:

Data Mining Techniques have become crucial identifying possible safety signals due to the growing availability of large –scale databases in pharmacovigilance .Large data sets can be used to find patterns and trends using these techniques ,which makes it possible to recognize possible links and hazards. Cluster analysis, association rule mining ,and disproportionality analysis,are a few popular data mining techniques.[34]

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A Statistical Technique called proportionality analysis is employed to pinpoint drug – event combination that have remarkably elevated frequency. Using null hypothesis of no connection , this method assesses the reported adverse events and contrasts the observed and expected frequencies.[34]

By putting comparable adverse occurrences together ,cluster analysis offers a technique to identify patterns that would not be seen when looking at individual case .This method aids in the identification of putative signals that have similar qualities ,like clinical signs , time-to-onset, or demographic traits.[34]

Data analysis for pharmacovigilance also used association rule mining.Using drug-event combinations as a starting point, this approach can be used to find hidden patterns and possible warning signs .[34]

III. CONCLUSION

In conclusion , the drug safety and pharmacovigilance are crtical components of the drug development and post-marketing surveillance process ,ensuring the protection of public health and the safe use of medications .The evolution of pharmacovigilance has led to the development of advanced signals detection methods ,real-world evidence ,and personalized medicine approaches .Despite challenges and limitations ,the integration of innovative technologies ,data analytics ,and collaborative strategies will continue to enhance drug safety monitoring and risk management .As the landscape of drug development and health care continues to evolve the importance of pharmacovigilance and drug safety will only continue to grow ,ultimately improving patients outcomes and public health. By prioritizing drug safety and pharmacovigilance, we can ensure that medications are used effectively and safely ,leading to better health outcomes and improved quality of life."

IV. REFERENCES

[1] Jeetu G, Anusha G1,Pharmacovigilance: A Worldwide Master Key for Drug Safety Monitoring,J Young Pharm Vol 2 / No 3, DOI: 10.4103/0975-1483.66802

[2] Geneva: World Health Organization. Looking at the Pharmacovigilance: ensuring the safe use of medicines. WHO Policy Perspectives on Medicines. Geneva: WHO; 2004. Available from: http://www.whqlibdoc.who.int/hq/2004/WHO_EDM_2004.8.pdf. [cited on 2009 Dec 15]

[3] Cioms CH. Geneva. Benefit-risk balance for marketed drugs. Evaluating safety signals: Report of CIOMS working group IV. CIOMS, Geneva. 1998. Available from: http://www.cioms.ch/publications/g4-benefit-risk.pdf. [last cited on 2010 Jan 15

[4] JAYESH KM RAJGOPAL*, KAJAL SHILPI, SRIVASTAV AK, PHARMACOVIGILANCE: A REVIEW ARTICLE, Innovare Journal of Medical Science, Vol 4, Issue 4, 2016,Received: 10 June 2016, Revised and Accepted: 22 July 2016

[5] Vipin Kesharwani*1, Mohd. Asad Farooqui1, Nikhil Kushwaha1, Ravi Kesh Singh1, Pankaj Kumar Jaiswal2, AN OVERVIEW ON PHARMACOVIGILANCE: A KEY FOR DRUG SAFETY AND MONITORING, Review Article,Journal of Drug Delivery and Therapeutics, Article Info: Received 02 Aug, 2018; Review Completed 09 Sep 2018; Accepted 10 Sep 2018; Available online 15 Sep 2018 DOI:http://dx.doi.org/10.22270/jddt.v8i5.1970

[6] Shuka SS, Gidwani B, Pandey R, Rao SP, Singh V, Vyas A, Importance pharmacovigilance in Indian Pharmaceutical Industry, Asian Journal of Research in Pharmaceutical Science 2012; (2):04-08.

[7] Lazarou J, Pomeranz BH, Corey PN, Incidence of adverse drug reactions in hospitalized patients, JAMA, 1998; 279:1200–1205.

[8] Bord CA, Rachl CL, Adverse drug reactions in United States hospitals. Pharmacotherapy, 2006; 26(5):601–08.

[9] Maiti B, Nagori B.P., Singh R, Kumar P, Upadhyay N, Recent Trends in Herbal Drugs: A Review, International Journal of Drug Research and Technology, 2011; 117-25.

[10] Rohilla A, Kumar V, Sharma KM, Dahiya A, Kushnoor A, Pharmacovigilance: Needs and Objectives, Journal of Advanced Pharmacy Education & Research, 2 Oct-Dec 2012;201-205.

[11] Rama P, Prudence AR, Georgy A, Pharmaovigilance: Perspectives and Future Challenges in Indian Scenario, Asian Journal of Pharmaceutical and Clinical Research, 2011; 4:01-04.

[12] Leon L, Herbert A. Liberman, Joseph L. Kanig, Varghese Publishing House, Hind Rajasthan Building Dadar, Mumbai, 3rdEdition, 239-240

[13] Ritu Rani *, Subhash Chand, Meena Devi, Arjun Singh, Deovrat Kumar, A Review on Signal in Pharmacovigilance, A R T I C L E I N F O:Asian Journal of Pharmaceutical Research and Development, Received 21 July. 2019; Review Completed 15 Sept. 2019; Accepted 25 Oct. 2019; Available online 15 Dec. 2019,DOI: http://dx.doi.org/10.22270/ajprd.v7i6.591

[14] ADRs reporting systems and signal detection. Viewpoint, Part 2, the Uppsala Monitoring Centre. 2005

[15] Mubasheera Mg, Pharmacovigilance (PV) continue signal detection, Department of Pharmacy, Nov-20, 2007

[16] Kumar anoop, Khan Henna, Signal detection and their assessment in Pharmacovigilance, Departmental of pharmaceutical science. Open pharmaceutical science journal, 2015; 2:66-73

[17] Ronald H.B. Meyboom,1,2,3 Marie Lindquist,1 Antoine C.G. Egberts 2,4 and I. Ralph Edwards, Signal Selection and Follow-Up in Pharmacovigilance, Drug Safety 2002; 459-465.

[18] CIOMS working Group. Practical aspects of signal detection in pharmacovigilance. Geneva; 2010(8)

[19] Anoop Kumar1,* and Henna Khan2, Signal Detection and their Assessment in Pharmacovigilance , Open Access, Open Pharmaceutical Sciences Journal, 2015, 2, 66-73 Received:February 06,2015,Revised:June 11,2015 Approved:October 27,2015

[20] Pirmohamed M, Sally J, Shaun M, et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. BMJ 2004; 329: 15-9.

[21] Dal Pan GJ. Ongoing challenges in pharmacovigilance. Drug Saf 2014; 37: 1-8

[22] Patel KJ, Kedia MS, Bajpai D, Mehta SS, Kshirsagar NA, Gogtay NJ. Evaluation of the prevalence and economic burden of adverse drug reactions presenting to the medical emergency department of a tertiary referral centre: a prospective study. BMC Clin Pharm 2007; 7: 1-5.

[23] Meyboom RH, Egberts AC, Edwards IR, Hekster YA, de Koning FH, Gribnau FW. Principles of signal detection in pharmacovigilance. Drug Saf 1997; 16: 355-65

[24] World Health Organization (WHO) guidelines on safety monitoring of herbal medicines in pharmacovigilance systems, World Health Organization, Geneva: WHO 2004

[25] Honig PK. Advancing the science of pharmacovigilance. Clin Pharmacol Ther 2013; 93: 474-75

[26] Meyboom RHB, Egberts ACG, Edwards RI, Hekster YA, Koning FHP, Gribnau FWJ. Principles of signal detection in Pharmacovigilance. Drug Sef 1997; 16: 355-65

[27] Inman WHW, Eds. Monitoring of drug safety. Lancaster: MTP Press 1986

[28] Van Grootheest K, Olsson S, Couper M, de Jongvan den Berg L.Pharmacists' role in reporting adverse drug reactions in an international perspective. Pharmacoepidemiol Drug Saf 2004; 13: 457-64

[29] Van Grootheest AC, Passier JL, van Puijenbroek EP. Direct reporting of side effects by the patient: favourable experience in the first year. Ned Tijdschr Geneeskd 2005; 149: 529-33

[30] Inman WHW, Rawson NSB, Wilton LV. Prescription event monitoring. In: Monitoring for drug safety. 2nd ed. MTP Press, Lancaster, England 1986: pp. 213-36

[31] Coulter DM, Edwards IR, McQueen EG. Post marketing surveillance in the general population-New Zealand. Monitoring for drug safety, 2nd ed. MTP Press: Lancaster, England, 1986: pp. 119-34

[32] ICH Tripartite Guideline, Pharmacovigilance Planning E2E, 2004. ICH E2E [online]. Available from URL: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2E/Step4/E2E_Guideline.pdf

[33] Klepper MJ. The periodic safety updates report as a pharmacovigilance tool. Drug Saf 2004; 27: 569-78

[34] JOSE ROSSELLO-1, Signal Analytics Technology in Pharmacovigilance: Enhancing Drug Safety Monitoring, April 6,2024.

[35] Bhanushali Mayank Ratilal1, Dr. Anuradha P. Prajapati2, Dr. Kantilal Narkhede3, Dr. Sachin B. Narkhede4, Dr. Shailesh Luhar5, A REVIEW ON PHARMACOVIGILANCE AND DRUG SAFETY MEASURES,EPRA International Journal of Research and Development (IJRD) Volume: 8 | Issue: 12 | December 2023 ,Article DOI:https://doi.org/10.36713/epra15259 DOI No: 10.36713/epra15259 , ISSN: 2455-7838(Online).

[36] Santosh, K. C., & Tragulpiankit, P. (2011). Pharmacovigilance: an overview. Mahidol Univ J Pharmaceutical Sci, 38(1-2), 1-7

[37] Kaeding, M., Schmälter, J., & Klika, C. (2017). Pharmacovigilance in the European Union: practical implementation across member states. Springer Nature

[38] Schatz, S., & Weber, R. J. (2015). Adverse drug reactions. Pharmacy Practice, 1(1).

[39] Meyboom RHB, Egberts ACG, Gribnau FWJ, Hekster YA. Pharmacovigilance in perspective. Drug Safety 1999; 21(6): 429-447

[40] I. Lakshmi Anusha*, M. Aashritha, K. Teja and R. Sridhar, A REVIEW ON PHARMACOVIGILANCE AND ITS IMPORTANCE, Review Article, WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES, Volume 6, Issue 1, 300-310 , ISSN 2278 – 4357, Article Received on15 Nov. 2016,Revised on 05 Dec. 2016,Accepted on 25 Dec. 2016 DOI: 10.20959/wjpps20171-8280

[41] Alexandra C. Păcurariu, The role of signal detection in Pharmacovigilance, ISBN: 978-94-028-0990-9,519883-L -sub01-bw-Pacurariu,Processed on: 5-6-2018.

[42] Eichler H-G, Oye K, Baird LG, Abadie E, Brown J, Drum CL, et al. Adaptive licensing: taking the next step in the evolution of drug approval. Clin Pharmacol Ther. 2012 Mar;91(3):426–37.

[43] Meagher E. Efficient drug approval and monitoring must rely on sound regulatory science : Nature Medicine : Nature Research [Internet]. [cited 2017 Feb 12]. Available from: http://www.nature.com/nm/journal/v17/n12/abs/nm1211-1535.html.

[44] Stricker BHC, Psaty BM. Detection, verification, and quantification of adverse drug reactions. BMJ. 2004 Jul 3;329(7456):44–7.