ISSN: 2230-7346

Krupa C. Thula et al. / JGTPS / 6(1)-(2015) 2351 – 2356

(Review Article)

Journal of Global Trends in Pharmaceutical Sciences

Journal home page: www.jgtps.com

REGULATORY REQUIREMENTS OF PHARMACOVIGILANCE SYSTEM AND ITS COMPARISON IN INDIA AND USA

Bhargavi H. Jadav[1], Krupa C. Thula[1*], Dilip. G. Maheshwari[2]

[1]Department of Quality Assurance and Pharm Regulatory Affairs, L. J. Institute of Pharmacy, Ahmedabad, Gujarat 382210, India.

[1]Assistant Professor, Department of Quality Assurance and Pharm Regulatory Affairs, L. J. Institute of Pharmacy, Ahmedabad, Gujarat 382210, India.

[2]Head of Department of Quality Assurance and Pharm Regulatory Affairs, L. J. Institute of Pharmacy, Ahmedabad, Gujarat 382210, India.

ABSTRACT

Pharmacovigilance system is a branch of pharmacological sciences dealing with reporting of Adverse Reaction Events which are caused by medicines and/or medical devices. Adverse Event caused is one of the potential concerns of public health which requires continuous recording, evaluation and monitoring. After the sulphanilamide tragedy in 1937 and the thalidomide disaster in 1960, Drug Regulations have been improved as well as have become stricter. As a result Pharmacovigilance System has been established which deals with collection, detection, assessment, monitoring and prevention of adverse effects of pharmaceutical products. India has Pharmacovigilance system which is regulated by Central Drug Standard Control Organization-CDSCO and US pharmacovigilance system is regulated by US Food and Drug Administration-USFDA. India has Pharmacovigilance Programme for monitoring adverse incidence related to medicines. United States also has firm regulations to improve Food and Drug Regulations for Pharmacovigilance. World health organization-WHO started International Monitoring System in collaboration with Uppsala Monitoring Centre-UMC. It is having worldwide database of adverse events which are recorded from among the member states of WHO-UMC. This article will focus on the pharmacovigilance programme in India depicting its Adverse Drug Reaction Reporting system, Pharmacovigilance in USA describing its ADRs Reporting System and comparison of pharmacovigilance regulations.

Key Words: Pharmacovigilance, Adverse Drug Reactions-ADRs, CDSCO, US-FDA, WHO-UMC

INTRODUCTION:

Pharmacovigilance-PV or Drug Safety is the branch of pharmacological science which deals with the collection, detection, assessment, monitoring and prevention of adverse effects of pharmaceutical products. The etymological origins for the Pharmacovigilance are: Pharmakon = drug in Greek language, Vigilare = to keep watch in Latin and As per WHO, Pharmacovigilance (PV) is defined as the sciences and activities, connecting to the finding, evaluation, understanding and prevention of adverse effects or any other drug-related problem. Before a product is marketed, experience of its safety and efficacy is limited to its use in clinical trials, which do not reflect practice conditions as they are limited by the patient numbers and duration of trial as well as by the highly controlled conditions in which Clinical Trials are conducted.

Address for correspondence

Krupa Chaitanyakumar Thula*
Assistant Professor,
Department of Quality Assurance and Pharm Regulatory Affairs, L. J. Institute of Pharmacy, Ahmedabad.
Mobile: +91-98986-60011
E-Mail: krupathula@yahoo.com

Pharmacovigilance is as a result one of the significant post-marketing tools in ensuring the safety of pharmaceutical and related health products. Apart from Drug Regulating Authorities Central Drug Standard Control Organization-CDSCO for India and US-Food and Drug Administration-USFDA for US, International Conference On Harmonization Of Technical Requirements For Registration Of Pharmaceuticals For Human Use, Pharmacovigilance Planning-ICH E2E and World Health Organization-Uppsala Monitoring Centre-WHO-UMC also play contributes for developing, Enhancing and Monitoring Pharmacovigilance System around the globe.

Pharmacovigilance and India:-

History:-[1], [2]

In **1986,** India proposed Adverse Drug Reaction Monitoring System (ADR monitoring System). It had 12 regional centers. Indiajoined World Health Organization-WHO-ADR Monitoring Programme in**1998**. In **2004-08**, India had started National Pharmacovigilance Programme which was performing under 2 Zonal, 5 regional and 24 Peripheral Regions. Currently India is having

Pharmacovigilance Programme of India which has commenced from 2010.

Pharmacovigilance Programme of India (PvPI):

It is 5 year programmed and it comprises of 5 phases:- Initial Phase (2010-11), Expansion and Consolidation phase (2011-12), Expansion and maintenance phase (2012-13), Expansion and optimization phase (2013-14) The Excellence Phase (2014-15)

Scope:-[2], [3]

Due to considerable social and economic consequences of adverse drug reactions there is a need to engage health-care professionals and the public at huge, in a well-structured programme to build collaborations for monitoring adverse drug reactions.

Purpose:-[2], [3]

The purpose of the programme is to assemble data, examine it and use the inferences to recommend informed regulatory interventions, besides interconnecting risks to healthcare professionals and the public.

The Pharmacovigilance Programme has the following signposts: To nurture a culture of notification, To engross several healthcare professionals and NGOs in the drug monitoring and information distribution processes, To achieve such operational efficiencies that would make Indian Pharmacovigilance Programme a benchmark for global drug monitoring endeavors.

Regulations:-[2], [3]

The Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services under the aegis of Ministry of Health & Family Welfare, Government of India in partnership with Indian Pharmacopeia commission, Ghaziabad has initiated a nation-wide Pharmacovigilance Programme for protecting the health of the patients by guaranteeingdrug safety. The Programme is being coordinated by the Indian Pharmacopeia commission, Ghaziabad works as a National Coordinating Centre (NCC). The centre operates under the supervision of a Steering Committee.The programme is coordinated by the National Pharmacovigilance Centre (NPC) at CDSCO. The National Centre will operate under the supervision of the National Pharmacovigilance Advisory Committee (NPAC) to recommend procedures and guidelines for regulatory interventions. The Pharmacovigilance programme of India encourages reporting all the suspected adverse reaction related to drug which also includes of those suspected to have been caused by herbal, traditional or alternative remedies. Any health care professionals (Doctors including Dentists, Nurses, and Pharmacists) may report suspected adverse drug events. Suspected adverse drug events are report through ADR reporting form. After completion the form shall be returned/ forwarded to the same Pharmacovigilance Centre from where it was received.

ADR Reporting Procedure of India:- [4], [5]

In India Reporting of ADR is done through following three ways under PvPI:

1. Healthcare Professional
2. Consumer Reporting
3. Public Health Programme-PHP

The reports are recorded through ADR reporting form by ADR monitoring centre /National Co-ordination Centre. Then they are entered into the vigiflow software and reports re-checked for it completeness. The access of report in vigiflow creates WORLWIDE UNIQE NUMBER.AMC personnel ensure the completeness and quality of the report and Causality assessment is done by Centre Co-ordinator/Deputy Co-ordinator. Technical assessment is performed and follow-up is also done. Hard copy as well as soft copy is preserved and their access is restricted. Reporting through Consumer and Public Health Programme are described in following chart.

Pharmacovigilance and USA:-[1, 5-14]

History:-[1], [5], [6]

After the Elixir Tragedy in 1937 and The Thalidomide Tragedy in1960 United States have revised the **Food and Drug Administration Regulations** to demonstrate the safety and efficacy of drug before issuing marketing authorization.

Regulations:-[7]

U.S. Department of Health and Human Services and Food and Drug Administration – FDA regulates pharmacovigilance with help of Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER).

ADR Reporting procedure of USA:-[7-14]

In USA, Adverse Drug Reactions are reported according to the Post Marketing Reporting of ADRs 21 CFR 314.80 to US Food and Drug Administration and FDA submit the Reports to the FDA Adverse Event Reporting System-FEARS. Reporting of ADR is done through following ways: Healthcare Professionals (Physicians, Pharmacists, Nurses and Others), Consumers (Patients, Family Members, Lawyers and Other), Regulated industries, Facility Users. Healthcare professionals, consumers, Regulated Industry and User facilities record the ADRs through either ADR form 3500A or ADR form 3500B and send these reports to FDA. Reporting is done online through MadWatch. FDA sends ADRs report to FDA Adverse Event Reporting System. Reports are assessed by clinical reviewers in the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). If a probable safety concern is acknowledged by FAERS, supplementary evaluation is performed this evaluation might include conducting studies using other large databases. The records are maintained for 10 years.

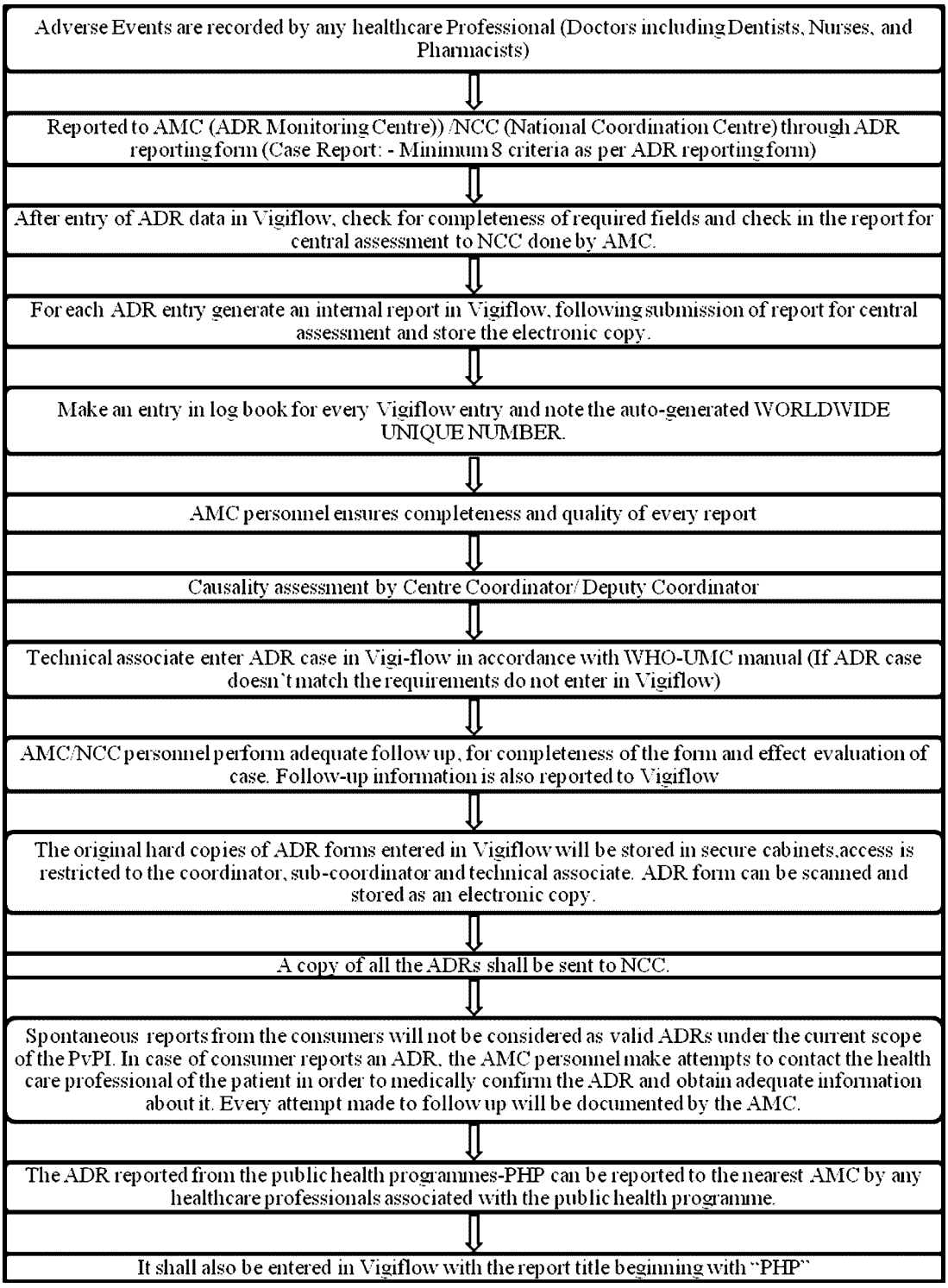

Figure 1. ADRs Reporting System of INDIA

Healthcare Professionals (Physicians, Pharmacists, Nurses and Others) and Consumer (Patients, Family members, Lawyers and other) submits the two copies of each Post marketing ADRs report to the FDA (*Post-marketing 15-day "Alert reports" and Post-marketing 15-day "Alert reports"—follow-up)* along with scientific Literature.

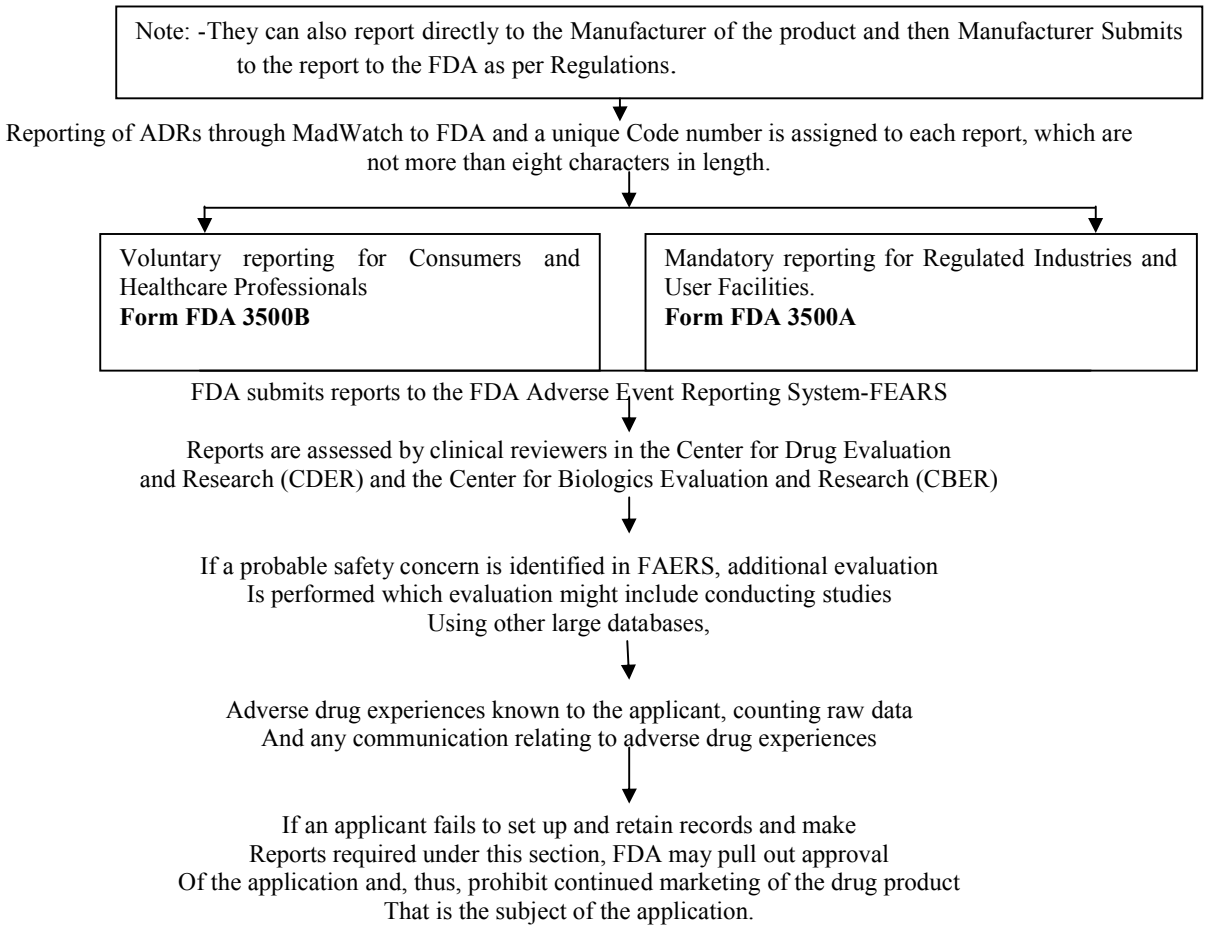

Figure 2: ADR Reporting System of USA

Pharmacovigilance and World Health Organization-WHO:-[2], [14]

After the thalidomide disaster in 1961, WHO established itsProgramme for International Drug Monitoring jointly with the WHO Collaborating Centre for International Drug Monitoring, WHO promoted Pharmacovigilance-PV at the country level. At the end of 2010, 134 countries were part of the WHO-PV Programme. The aims of PV are, to augment patient care and patient safety in relation to the use of medicines; Toupkeep public health programmes by providing reliable, balanced information for the effective assessment of the risk-benefit profile of medicines. UMC manages chief aspects of the mounting universal Pharmacovigilance set-up of the now more than 130 countries, known as the WHO Programme for International Drug Monitoring. WHO Collaborating Centre follows WHO policies and work in close relation with it does headquarter. UMC is organisationally and professionally discrete from WHO itself. The WHO Program for International Drug Monitoring offers a forum to the member states of WHO in the monitoring of drug safety. The individual case reports of ADRs are collected under this program and stored in one common database. Currently it has more than 3.7 million case reports.

- The Uppsala Monitoring Centre is answerable for the collection of ADRs data from around the globe and especially from member states.
- Reports are sent to the UMC by member countries and here they are processed, evaluated and entered in to the WHO International database.
- After detailed evaluation and expert review there is availability of several ADRs reports to particular drug which leads to the detection of a signal that is an alert about a possible hazard communicated to the member countries.
- ADR reports are assessed locally and may lead to action within the country
- India has a large patient pool and healthcare professionals still ADR reporting is in its early years.

RESULT:

Table 1: Comparison of Regulation of Pharmacovigilance between INDIA and USA:[2-13]

S.no	Parameters	India	USA
1	Regulatory Authority	CDSCO	FDCA and FDA implementing regulations
2	Pharmacovigilance Responsible Authority	National Co-ordination centre	CDER and CBER
3	Guidelines	Pharmacovigilance Programme India Follow PSUR and ADR reporting as per Schedule Y	Guidance for Industry Good Pharmacovigilance Practices and Pharmaco-epidemiologic Assessment
4	Process For Pharmacovigilance Filling	National Authorization Process	FDA Adverse Event Reporting System (FAERS)
5	Pharmacovigilance system and Quality	No specific Module is available	No specific module is available
6	Pharmacovigilance System Master File-PSMF	Not Required	Not Mentioned
7	Pharmacovigilance Inspection	Not Mentioned	Mentioned in Post-marketing Adverse Drug Experience (PADE) Reporting Inspection.
8	Pharmacovigilance Audit	Not Mentioned	----------
9	Risk management System	Risk Management System is given in PvPI	Risk Management System is given in Risk Management Guidance under Guidance for Industry, Good Pharmacovigilance Practice and Pharmacoepidemiologic assessment.
10	Adverse Drug Reaction	PvPI and Schedule Y give information related to ADR	In Sec. 314.80 Post-marketing reporting of adverse drug experiences.
11	Serious ADR reporting time period	Within 15 days	Within 15 days.
12	Non Serious ADR reporting time period	Not required on serious basis	-
13	Database	Vigiflow software	FEARS for small database and Sentinel System for Large database
14	Forms	Only one ADR form is available for reporting all products	1. Voluntary reporting for Healthcare professionals and consumers through ADR form 3500B 2. Mandatory Reporting for Regulated industry and facility User through ADR form 3500A
15	Periodic Safety Update Report-PSUR	They require format as per ICH E2C	They require format as per ICH E2C
16	Data Lock Point for PSUR	60 days	70/90 days
17	Safety Communication	Not mentioned	Mentioned in Guidance for Industry, E2E Pharmacovigilance planning.
18	Risk Minimization Measure	Not mentioned	Risk Minimization is done through Risk Minimization Action Plans-RiskMAP guidelines.

CONCLUSION:-

The article gives brief overview about Adverse Drug Reactions reporting system of Pharmacovigilance in India as well as USA. India has started 5 phased Pharmacovigilance programme of India which is in collaboration with WHO-UMC. In India Pharmacovigilance system is still in its infancy. It only provides facility for reporting adverse reaction caused by drugs. This will help to build up large ADRs database. Pharmacovigilance regulations of USA are well developed and stricter. They have two separate ADR reporting for applicant for reporting of Adverse Drug Reactions. WHO-UMC gives regulations for setting up Pharmacovigilance Plan in member state. It maintains one database which has Adverse Drug Reactions that has occurred around the globe among member state. The Pharmacovigilance system will help country to maintain the ADRs data which will beStored in one database and help to prevent and monitor further ADRs incidence.

ACKNOWLEDGMENT

The authors are thankful to Dr. K Pundarikakshudu, Director of L. J. Institute of Pharmacy, Ahmedabad, India for providing all the facilities and encouragement to carry out the research work.

REFERENCES

1. Indian Pharmacopoeia commission, Pharmacovigilance programme of India, http://ipc.nic.in
2. National Pharmacovigilance protocol, http://www.nlsenlaw.org/wp-content/uploads/2013/08/N ational-Pharmacovigilance-Protocol.pdf
3. All India Institute of Medical Science, Standard operating procedure for processing and reporting of Pharmacovigilance programme, http://www.aiims.edu
4. Central Drug Standard Control Organization-CDSCO, Pharmacovigilance programme of India, http://www.cdsco.nic.in/forms/cont
5. The Scientist, Sulfanilamide tragedy, http://www.the-scientist.com
6. Bhanu Prakash and Gurcharan Singh, PHARMACOVIGILANCE: SCOPE FOR A DERMATOLOGIST, Indian J Dermatol. 2011 Sep-Oct; 56(5): 490–493.
7. US Food And Drug Administration, guidance for Industry Good Pharmacovigilance Practices and Pharmacoepidemiological Assessment ,http://www.fda.gov/downloads/RegulatoryInformation/ Guidances/UCM126834.pdf
8. ADR REPORTING US Food And Drug Administration , CFR - Code of Federal Regulations Title 21, http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=314.80
9. US Food And Drug Administration, FDA Adverse Event Reporting System (FAERS), http://www.fda.gov
10. US Food and Drug Administration, Safety-Med watch, http://www.fda.gov/Safety/MedWatch/
11. US Food And Drug Administration, Inspection, http://www.google.co.in
12. US Food and Drug Administration, Providing Post-market Periodic Safety Reports in the ICH E2C(R2) Format (Periodic Benefit-Risk Evaluation Report), http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm346564.pdf
13. US Food and Drug Administration , E2E Pharmacovigilance Planning, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073107.pdf
14. World Health Organization-Uppsala Monitoring Centre, Pharmacovigilance, http://www.who-umc.org

How to cite this article:

Bhargavi H. Jadav, Krupa C. Thula*, Dilip. G. Maheshwari,: Regulatory requirements of Pharmacovigilance system and its comparison in INDIA AND USA, 6(1): 2351 - 2356. (2015)