

# Effective Communication in Pharmacovigilance: Role & Set Up

<sup>1</sup>Manish Kumar\*, <sup>2</sup>Rajneesh Garg, <sup>3</sup>HC Patil, <sup>4</sup>RK Patil

<sup>1</sup>Professor, Department of Pharmaceutics, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh Univeristy, Bathinda, 151001, Punjab, India.

<sup>2</sup>Associate Professor, Department of Pharmacognosy, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh Univeristy, Bathinda, 151001, Punjab, India

<sup>3</sup>Professor & Principal, Department of Pharmacy Practice, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh Univeristy, Bathinda, 151001, Punjab, India.

<sup>4</sup>Professor, Department of Pharmacy Practice, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh Univeristy, Bathinda, 151001, Punjab, India.

## ABSTRACT

Pharmacovigilance (PV) is known as the branch of science including activities related to the detection, evaluation, control and prevention of adverse drug reactions and its related problems including allergic reactions. The main concern of pharmacovigilance is the assessment of risk vs. benefit drug profile for better potency with more safety to use various drugs in patients suffering from several ailments. Pharmacovigilance plays a crucial role in the healthcare industry in the accountable use of drugs in the society by collecting data and providing reports on various adverse drug reactions among different users. Pharmaceutical industry in India, in the world is able to achieve 3<sup>rd</sup> place in terms of capacity and morals. New drug molecules including synthetic and herbal constituents, specific dosage forms and drugs are manufactured on large scale in India as a centre of choice for research and development. However we require a globally standardized pharmacovigilance system for better safety studies in Pharmaceutical industries. This review article enlightens the role of effective communication in pharmacovigilance and its importance in health industry.

**Keywords:** Drug development, Adverse event, Pharmacovigilance, Health Profession.

## 1. INTRODUCTION

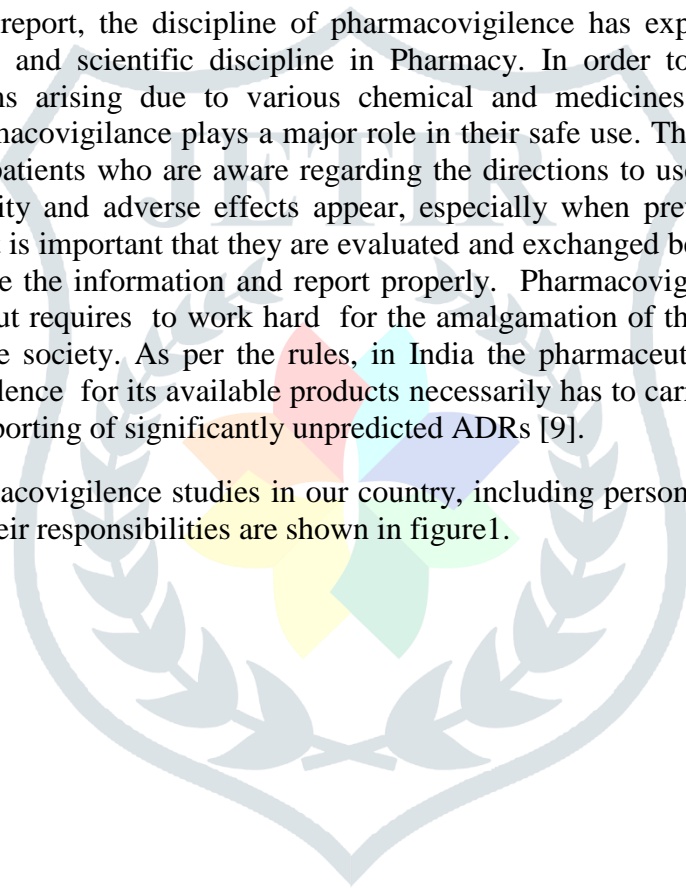
Pharmacovigilance (PV) was officially introduced in December 1961 by W. McBride, an Australian doctor through the publication of a case report in the well known journal Lancet, in which he suspected a connection between serious fetal deformities (phocomelia) and thalidomide, which was a drug of choice in pregnancy : Thalidomide was used as an antiemetic and sedative agent in pregnant women [1]. In 1968, the World Health Organisation (WHO) endorsed the “Programme For International Drug Monitoring”, a pilot project designed to centralize world data on adverse drug reactions (ADRs). The main object of the “WHO Programme” was to recognize the earliest possible pharmacovigilance signals. In the mid-70’s, a French group of pharmacologists and toxicologists suggested the term pharmacovigilance to define the activities promoting “The assessment of the risks of side effects potentially associated with drug treatment” [2]. Pharmacovigilance can be defined as the science of assembling, measuring, researching and evaluating information from healthcare providers and patients on the adverse events of various medicines, vaccines, toxoids, blood products, medical devices, traditional herbal and synthetic drugs with an aim to collect information about several threats associated with these molecules and prevention of harm to the patients. The challenge to maximize drug safety has become very difficult in order to maintain confidence of the society. The need of the hour is that Pharma Industries should actively evaluate and manage drug risks through a product’s lifecycle, in addition to monitor, from development to the postmarket [3]. Pharmacovigilance is markedly concerned with ADRs, which are unintended and poisonous responses of the drugs occurring at prophylaxis doses used normally for the diagnosis or treatment of illness, or for the moderation of the bodily functions [4]. Ongoing monitoring of drug effects, side effects, contraindications and absolute harmful effects which could lead to increased

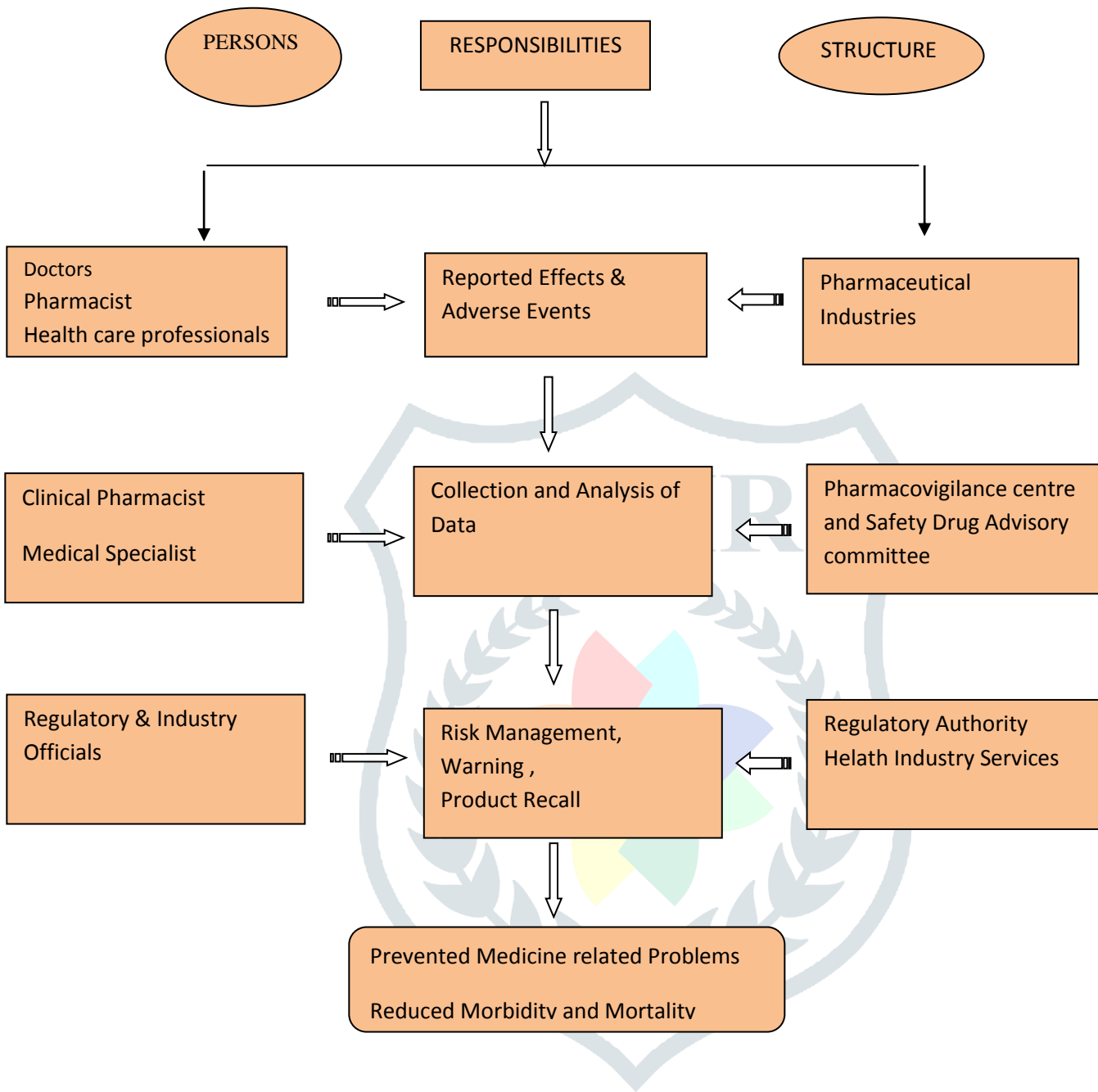
morbidity and mortality in some cases, are beneficial to amplify beneficial effects whereby reducing the risks. During pre-clinical and clinical studies including clinical trials, the utmost attention and awareness can guarantee an absolute safety, when a drug is marketed and prescribed to vast inhabitants. New drug molecules are launched in the market with very few side effects and Adverse drug reactions are frequently not known during that time, because the clinical trials involve at most several thousands of patients. Post marketing pharmacovigilance uses aid such as data mining and analysis of case reports to identify the correlation between drug and ADRs. It is the duty of the drug regulatory agencies to have a well-developed pharmacovigilance system to monitor ADRs during the drug development phase and later during the lifetime of a marketed drug [5]. The partners of drug safety monitoring practices such as government, industry, health care centers, health professionals, Pharmacists, patients have a typical connection in their survival. [6,7]. Continues coordination and adherence are essentially required in order to defeat Adverse events and meet future challenges in pharmacovigilance [8].

### 1.1 Scope of PV

Since 1972 WHO technical report, the discipline of pharmacovigilance has expanded substantially and it leftover an effectual clinical and scientific discipline in Pharmacy. In order to overcome inevitable and unpredictable potential harms arising due to various chemical and medicines of biological origin like vaccines, sera, toxoids, Pharmacovigilance plays a major role in their safe use. The use of drugs by qualified health professionals and by patients who are aware regarding the directions to use drugs reduces the risk of side effects. When the toxicity and adverse effects appear, especially when previously unknown with the medicine in the association, it is important that they are evaluated and exchanged beneficially to expert having the understanding to elucidate the information and report properly. Pharmacovigilance agent is responsible for this role upto a extent, but requires to work hard for the amalgamation of the discipline into Pharmacy Practice for beneficial of the society. As per the rules, in India the pharmaceutical industries, in order to accomplish the pharmacovigilance for its available products necessarily has to carry out the activities such as assemblage, and advanced reporting of significantly unpredicted ADRs [9].

A distinctive setup for pharmacovigilance studies in our country, including persons participating on different levels, structural units and their responsibilities are shown in figure1.





**Figure 1:** A typical pharmacovigilance setup

## 2. CLINICAL RESEARCH REGULATION IN INDIA

In our country there are a number of regulatory agencies which play their leading role in conducting clinical trial along with Ethics committee. These regulatory agencies are described in below mentioned table along with their role.

Agencies	Role of agencies
<b>Drug Controller General Of India (DCGI)</b>	DCGI Plays key role in implementation of National Pharmacovigilance Program (NPP)
<b>Central Drugs Standard Control Organisation(CDSCO)</b>	CDSCO is operating along with National Pharmacovigilance Advisory Committee to recommend regulatory procedures& guidelines
<b>Department of Biotechnology(DBT)</b>	DBT Provides support for pilot and large scale trials on agricultural and clinical trials for health care products evaluation and validation.
<b>Ministry of Environment and Forests(MOEF)</b>	MOEF advisory committee play a role in approving guidelines on data enteries of environmental experts information gained through the clinical trials for health care products and trials for agriculture products.
<b>Central Bureau of Narcotics (CBN)</b>	CBN regularly monitors clinical trials of Narcotics Drugs for compliances related to storage , import, export quotas and movement of drug under investigation.
<b>National Pharmacovigilance Advisory Committee(NPAC)</b>	NPAC aggregate, access and documents adverse drug reaction data to create friendly environment for the regulatory authorities to analyze the drugs before marketing.
<b>Indian Council of Medical Research (ICMR)</b>	ICMR in 1980 introduced the 'Policy Statement on Ethical Considerations involved in Research on Human Subjects' and revised these guidelines in 2000 as 'Ethical guidelines for Biomedical Research on Human Subjects'.
<b>Ministry of Health and Family Welfare(MHFW)</b>	MHFW sets standards for pharmaceuticals healthcare devices and medicines in India

Tab1: Regulatory agencies in India

## 3. Data Mining for PV

Pharmacovigilance in order to enhance patient safety and enhanced health care against various drugs used is divided into two different stages sch as

### Stage-I:

**Pre –Market Surveillance** - Involves collection of information regarding adverse drug reactions from Phase 1 to Phase 3 clinical trials

### Stage-II:

**Post –Market Surveillance-** Involves collection of data in the post approval stage through market to determine safety issues.

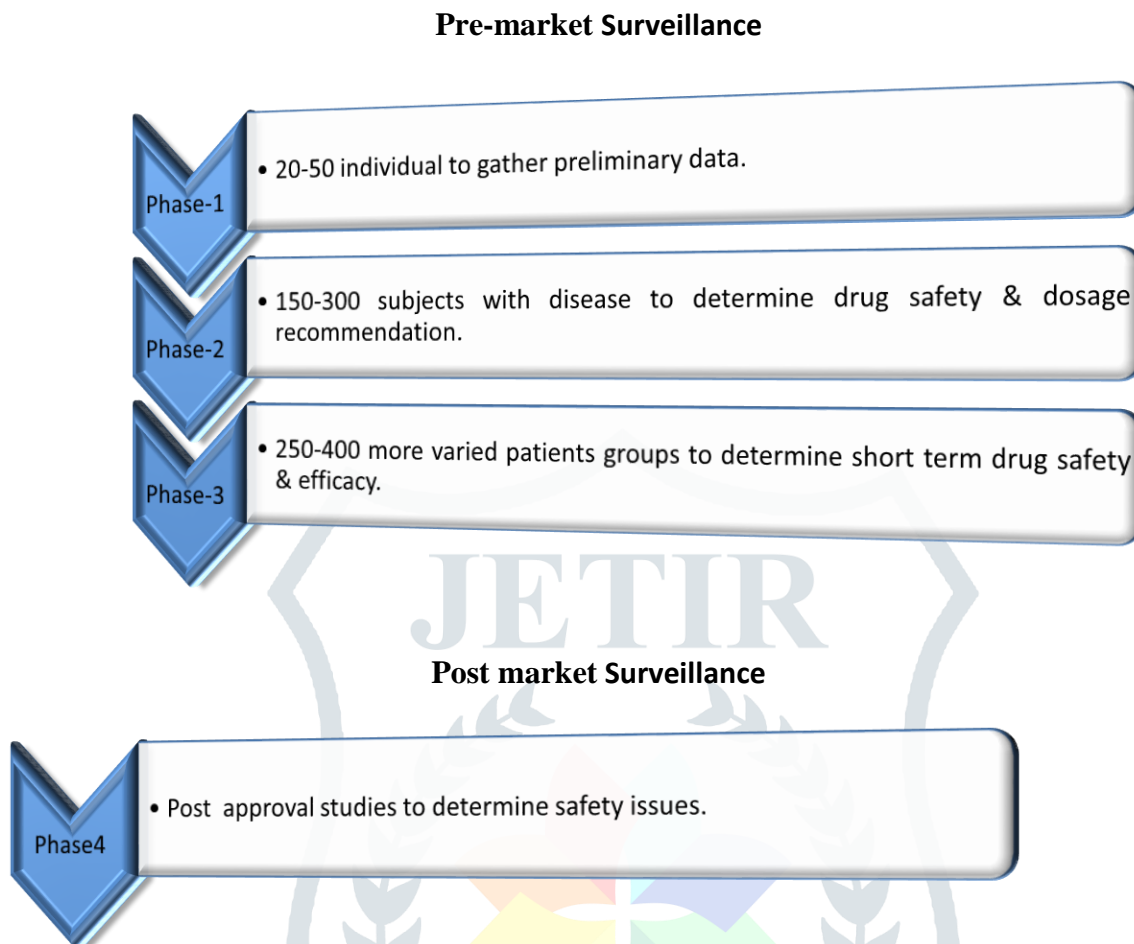


Figure 2: Pharmacovigilance at different stages of Drug Development & Registration

### 3.1 Premarket Surveillance

During the pre-marketing phase, pharmacovigilance has been devoted to speculate potential ADRs in the early stages of drug development process. Safety Pharmacology Profiling (SPP) is one of the basic methods most commonly employed in preclinical in-vitro assessment of compounds with the help of biochemical and tissue culture techniques at laboratory scale. This method works on the principle that in order for appearance of any ADR in human beings, a chemical moiety will bind to a specific target the result of which may produce any reported adverse effect. However, in economic and effective terms, an experimental reports of ADRs are not always acceptable. By using the preclinical characteristics of the compounds using SPP models, a wide range of research activities have been implemented to speculate most possible ADRs. The categorization of the current research is based on the protein targetting and chemical structural related approaches. [10].

### 3.2 Post-marketing surveillance

A drug undergoes a substantial clinical screening prior to its acceptance by the Food and Drug Administration (FDA), still there are chances to skip several ADRs as unnoticed due to small biased clinical trials by non-involvement of the patients suffering from concurrent diseases like insomnia, diabetes, anxiety and depression. One cannot rely on Premarketing clinical trials as they do not provide actual information for varied community, therefore the continuation of the post-market surveillance is essential. Pharmacovigilance plays a great role in evaluating post-marketing of newly developed drugs [11,12]. The competition among the different pharmaceutical industries along with the rigorous regulatory evaluation procedures allows a research and development process prior to the launch of a new drug into the market. Post marketing

pharmacovigilance is carried out by Various unique data sources [13]. The research of pharmacovigilance is based on an analysing “signals”. By the World Health Organisation, these signals are defined as unrevealed assertions on the direct correlation between the response on the patient and a drug to show unwanted effects [14]. The clinicians and researchers make an application of spontaneous reporting systems (SRS) for the generation of comprehensive signal datasets. In some European countries and the United States, the use of an electronic SRSs is already in place. Besides alternate remedies include Physicians database analysis ,post market surveillance of prescriptions are being thoroughly researched. However , the most of the data is not publicly available for the explorers which along with the other barriers, severely limits signal detection [15-17]. While the drug companies need to trace and manage the adverse event reports by the clinicians, lawyers or patients , the process of detection mainly depend upon an ability of recognition of given symptoms as a drug adverse event, by the physician. Since the problem of the collection and filtration of the ADR data from different nodes has already been studied in the past, clinicians continue to implement new strategies on collected data in conjunction with other post drug administration techniques [18]. Using different techniques capable of collecting medical records, PV clinicians are challenged with the problem of delivering knowledge-oriented tools and services which should help out to get best possible results with reduced unwanted effects from recorded databases. At the last , the elaboration and through analysis of the post market surveillance database will set up a foundation stone for pharmaceutical industries, Regulatory bodies, Health department and Research for improved drugs analysis[19].

#### 4. PHARMACOVIGILANCE STEPS<sup>20</sup>

The primary steps involved in pharmacovigilance are:

- Management of safety data
- Detection of Signal
- Signal evaluation and decisions in accord to safety measures
- Regulatory Actions to protect health of the community
- Providing Information

**Management of safety data:** Any drug molecule can cause severe untoward reaction either during pre market surveillance phase or during post marketing surveillance phase. The reporting of serious adverse reaction may be done by a doctor, a pharmacist, a nurse, patient himself, any relative or family member, neighbor or any paramedical staff. As these untoward effects of drug may occur any time during lifeperiod of drug molecule, so it's a requirement of time to properly monitor and manage the drug safety data.

The steps involved in management of safety data are:

- Collection and verification of data
- Adverse drug reactions coding
- Drugs coding
- Assessment of causalities
- Reporting to authorities

- **Collection and verification of data**

**Acknowledgement:** All authentic cases are required to be acknowledged properly by providing acknowledgement number to collect more information from the reporter as per requirements.

**Duplicate search:** There are a number of safety database softwares capable to search and differentiate duplicate reportings. Various factors like patient age, patient sex, date of drug exposure, country etc. are basic tools to find any duplicacy.

**Triage:** Triage is used to give priority to the case for reporting to authorities depending on reported deaths and life threatening adverse reactions within 7 days and non severe adverse reactions in 15 days.

**Data entry:** The authentic cases should be reported carefully. Patient information should be stored with utmost care and confidentiality. The information of the ADR reporter should be clear and detailed enough in order to make him approached easily if required. All the information regarding Drug like brand name, generic name, dosage form and dose must be recorded accurately. All side effects must be recorded in details in order to find the reason of the adverse drug reaction. This would include chronological details of the events, nature, severity, characteristics of the event, results of investigations and tests, starting date, treatment schedule and outcome, other associated medicines .

**Case narratives:** case narratives includes summary of a submitted case containing all the related information including drug and its ADRS. During management of safety data, case narratives are evaluated and used by case reviewers to decide seriousness of adverse events.

**Drugs Coding:** The suspected drug and the associated drugs are required to be coded. For the coding purpose most of the times drug dictionary provided by World Health Organization is used; which is updated three to four times in a year by pharmacovigilance monitoring centre of WHO. Various biotechnological including special products, blood products, diagnostic substances are also available in WHO dictionary. WHO drug record number system and ATC classifications are used respectively for chemical and therapeutic groupings.

**Causality assessment:** A causality assessment is required to be conducted in almost every cases especially in those cases where severity of adverse reaction is not confirmed due to administration of drug moiety. The precise measurement of the occurrence of a relationship between drug exposure and adverse events is carried out by several approaches based on the following considerations:

- The case history between drug administration and adverse events
- Possibility based on signs and symptoms, lab tests, MOA & Other information
- Knowledge of pharmacology and frequency of adverse reactions occurring due to the suspected drug
- Exclusion of the disease condition or concurrent medicines for similar adverse reactions.

**Reporting to authorities:** The reporting to the concerned authorities or stakeholders should be done at right time in order to fulfill the role and responsibilities of a pharmacovigilance agent. This will help in timely update of ADRs and issuance of safety guidelines of any pharmaceutical product post marketing surveillance.

## 5. EFFECTIVE COMMUNICATION IN PHARMACOVIGILANCE <sup>21</sup>

The active, timely and effective communication plays a major role in issuance of updates on guidelines on drug safety as per pharmacovigilance experts present in all around the world. Effective communication helps in creation of safety guidelines with the following statements:

- The safety information on all the drug molecules must be sufficiently collected, assessed and made easily accessible to all by each country.
- Drug safety information must be able to improve health of the community.
- Health care providers and public must be educated regarding appropriate use of drug molecules along with safety information.
- Free access to all the evidences required to assess and understand risks and benefits of drug
- Information and remedies are efficiently communicated

These factors will definitely help in generation of drug safety guidelines and evaluation of risk vs. benefits ratio of drug molecules.

## 6. List of Banned Drugs By CDSCO

Central Drugs Standard Control Organisation (CDSCO) has banned several drugs in India due to their potential risks to human life. Below mentioned table contains some of the drugs that have been banned in India along with ADRs reported.<sup>22</sup>

Drug Name	ADR Reported
Cisapride	Cardiac arrhythmias
Gatifloxacin formulation	hyperglycemia and liver damage
Terfenadine	Cardiac arrhythmias
Rofecoxib	Myocardial infarction w
Valdecoxib	Heart attack and stroke
Nimesulide formulations for human use in children below 12 years of age.	Hepatotoxicity
Tegaserod	Cardiovascular ischemic events occurred followed by heart attack and stroke
Cisapride and its formulations for human use	Irregular heartbeat, Cardiac arrest& Convulsions
Sibutramine and its formulations for human use.	Cardiovascular risk
Dextropropoxyphene and formulations	Cardiac toxicity

**Table 2:** List of drugs banned by CDSCO

## CONCLUSION

Pharmacovigilance is known as the branch of science including activities related to the accumulation, detection, evaluation, control and prevention of adverse drug reactions and its related problems including allergic reactions. PV analyst plays a major role in gaining information from healthcare personnel and patients on the adverse effects of medicines including biological products such as vaccines, toxoids, anti coagulants, herbs, medical devices, traditional and synthetic medicines to prevent harmful and life threatening effect of the drug moieties on the community. As pharmaceutical industrial field is growing day by day in our country, we require strong pharmacovigilance system for the monitoring of the adverse effects of drug and assuring patient safety. Despite of all the efforts made by CDSCO for the establishment of a global pharmacovigilance system for the country a lot of challenges need to be overcome for successful implementation of pharmacovigilance like lack of awareness among pharmacists, nurses, patients and shortage of technical staff for reporting ADRs. The need of the hour is to educate the physicians, pharmacist and nurses to encourage them to report ADRs that occur in patients. Standard guidelines for pharmacovigilance in India, inspired by the good pharmacovigilance practices devised by EMA, will truly serve the purpose of ensuring safety of our patients and establishing a global system for drug safety monitoring.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.



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