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## PHARMACOVIGILANCE: A COMPREHENSIVE REVIEW

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### ABSTRACT

Pharmacovigilance (PV) is an important area for the safety and ensuring that the patients are safe in every aspect of the drugs being taken or injected. Pharmacovigilance the science and series of activities relating to the detection, evaluation, understanding and avoidance of adverse effects or any other drug-related problem' plays an important role in ensuring that patients be given safe drugs. Nowadays in India pharmacovigilance gives awareness about adverse drug reactions (ADR) and this review gives information about implementation for solving current problems. The present review presents in brief about the relevance, need, functioning, role, and importance of pharmacovigilance.

**KEYWORDS:** Pharmacovigilance, Adverse drug reaction, Clinical trial, Drug safety.

### INTRODUCTION

The term "Pharmacovigilance" first appeared in French in the late 1960s, when the term "Pharmacovigilance intensive and Pharmacovigilance spontanee" were contrasted.<sup>[1]</sup> Drug safety and Pharmacovigilance remains a dynamic clinical and scientific discipline.<sup>[2]</sup> <sup>[3]</sup> According to WHO, Pharmacovigilance (PV) as the pharmacological science and activities relating to the monitoring, detection, assessment, understanding and prevention of adverse drug reaction or any long term and short term medicines related problem.<sup>[4]</sup> Pharmacovigilance is highly regulated in major regions of the world where medicines are developed. <sup>[5]</sup>

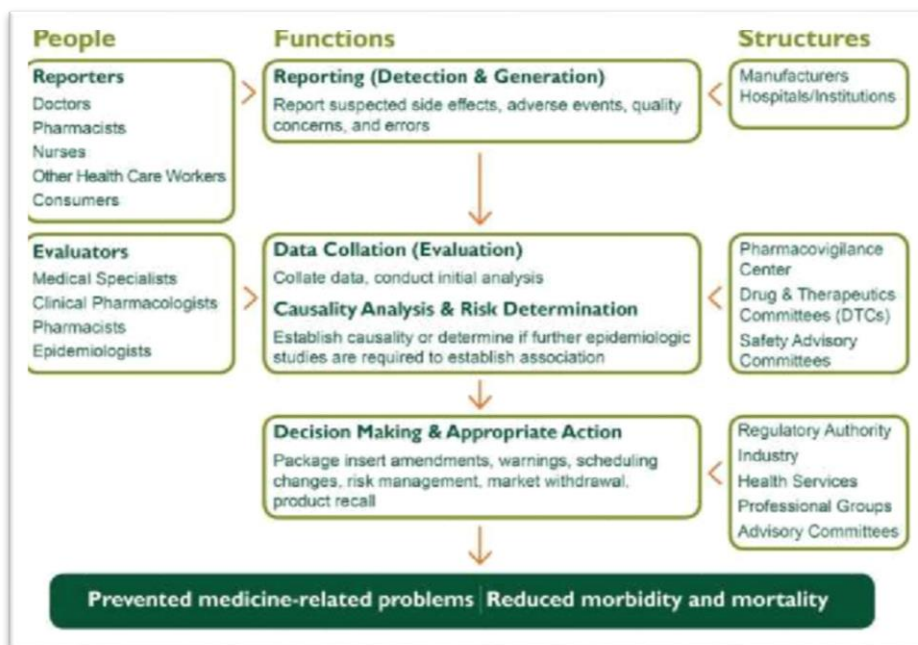


Figure no 1: Pharmacovigilance Framework. [4]

India with a current population of 1.27 Billion, is that the fourth largest producers of prescription drugs within the worlds with quite 6,000 licensed markers and over 60,000 branded formulation within the market. In the united State of America, ADRs contributes 3-7% of hospital admission. In England 1% chronicles of the entire hospital admission where due to ADRs throughout the Year 1999-2001. [4]

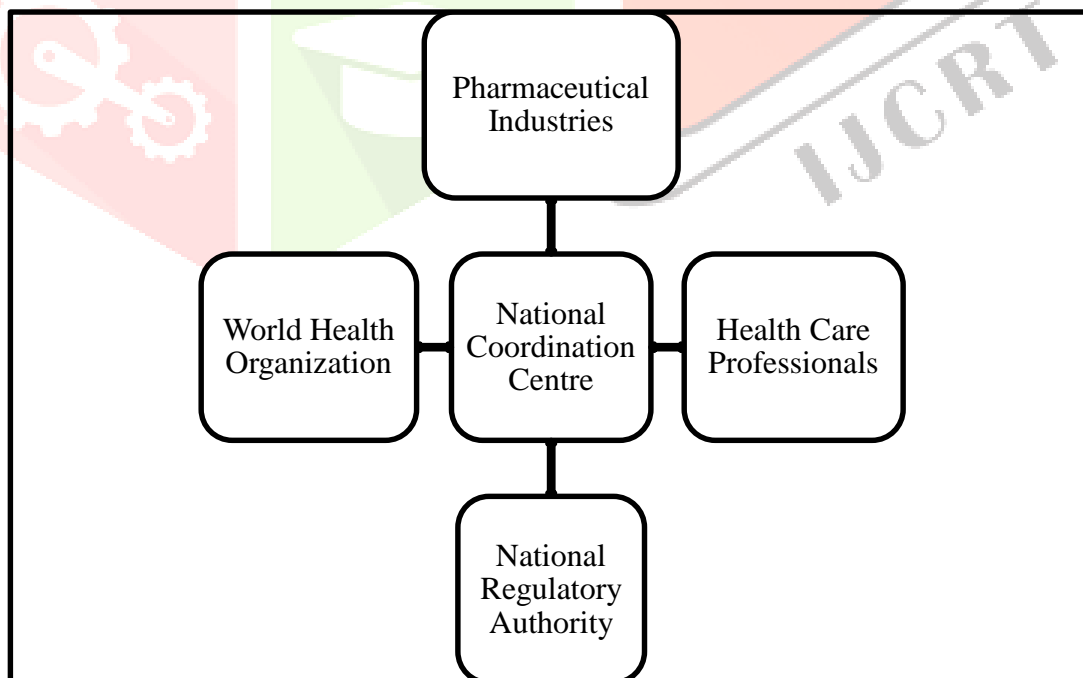


Figure no 2: Diagrammatic representation of the pharmacovigilance

## HISTORY OF PHARMACOVIGILANCE IN INDIA

Pharmacovigilance in India started from 1986. A formal Adverse Drug Reactions (ADR) monitoring system was initiated with 12 regional centres, each covering a population of 50 million. However, no noteworthy growth was made. Afterward in 1997, India joined World Health Organization (WHO) and Adverse Drug Reaction (ADR) scrutinizing programme based at Uppsala, Sweden but got fail. Hence, after 2005 WHO supported and World Bank –funded National Pharmacovigilance Programme (NPPV) of India was made operational.

Table no 1: The Sequential Pharmacovigilance Developments With Special Reference To India. <sup>[6]</sup>

Developments	Year
First clinical trial was done by James Lind. providing the usefulness of lemon juice in preventing scurvy.	1747
Due to toxicity of sulfonamide death of more than 100 children occurred.	1937
Due to toxicity of chloramphenicol aplastic anemia reported.	1950
Worldwide tragedy due to thalidomide toxicity.	1961
16 <sup>th</sup> World Health congregation recognize significant to rapid action on Adverse Drug Reaction (ADRs)	1963
WHO research project for international drug monitoring on pilot scale.	1968
Global standard level clinical trials initiated in India.	1996
India attached with WHO, Adverse Drug Reaction Monitoring program.	1997
Initiation of pharmacovigilance in India.	1998
67 <sup>th</sup> National pharmacovigilance centre established in India.	2002
India launched National pharmacovigilance program.	2004-05
Accomplishment of structured clinical trials in India.	2005
Pharmacovigilance program (PvPI) started.	2009-10

## GOAL

Pharmacovigilance has an important role in the assessment of side effects caused by the drugs whether it is caused by oral drugs; parenteral drugs or I.V. drugs. These drugs are pretested for ADRs before it is being marketed worldwide. PV has a key role in assessment, detection and identification of drugs which caused a particular ADRs and the mechanism by which it caused the injury. But to fulfill these requirements of finding and eliminating, a side effect is the responsibility of the doctors involved in the case; nurses, health workers, residents and proper guidance of the patients themselves help it to alleviate the root cause of ADR pharmacovigilance promote understanding education and clinical training in pharmacovigilance and its effective communication to the public <sup>[7]</sup>. PV has an important role in the assessment of side effect caused by the drug whether it is caused by oral drug parenteral drug, iv. <sup>[8]</sup> Preventing patients from being affected unnecessarily <sup>[9]</sup>

## OBJECTIVE

The main objectives of pharmacovigilance involve exhibiting the efficacy of drugs by monitoring their adverse effect profile for many years from the lab to the pharmacy; tracking any drastic effects of drugs improving public health and safety in relation to the use of medicines; encouraging the safe, rational and

cost-effective use of drugs; promoting understanding, education and clinical training in pharmacovigilance; and effective communication to the general public. <sup>[4] [10]</sup>

1. To create a nation-wide system for patient safety reporting.
2. To identify and analyse the new signal (ADR) from the reported cases.
3. To generate the evidence-based information on safety of medicines.
4. To analyse the benefit-risk ratio of marketed medications.
5. To support regulatory agencies in the decision-making process on use of medications.
6. To communicate the safety information on use of medicines to various stakeholders to minimise the risk.
7. To emerge as a national centre of excellence for pharmacovigilance activities.
8. To provide training and consultancy support to other national pharmacovigilance.
9. To collaborate with other national centres for the exchange of information and data management. <sup>[10]</sup>

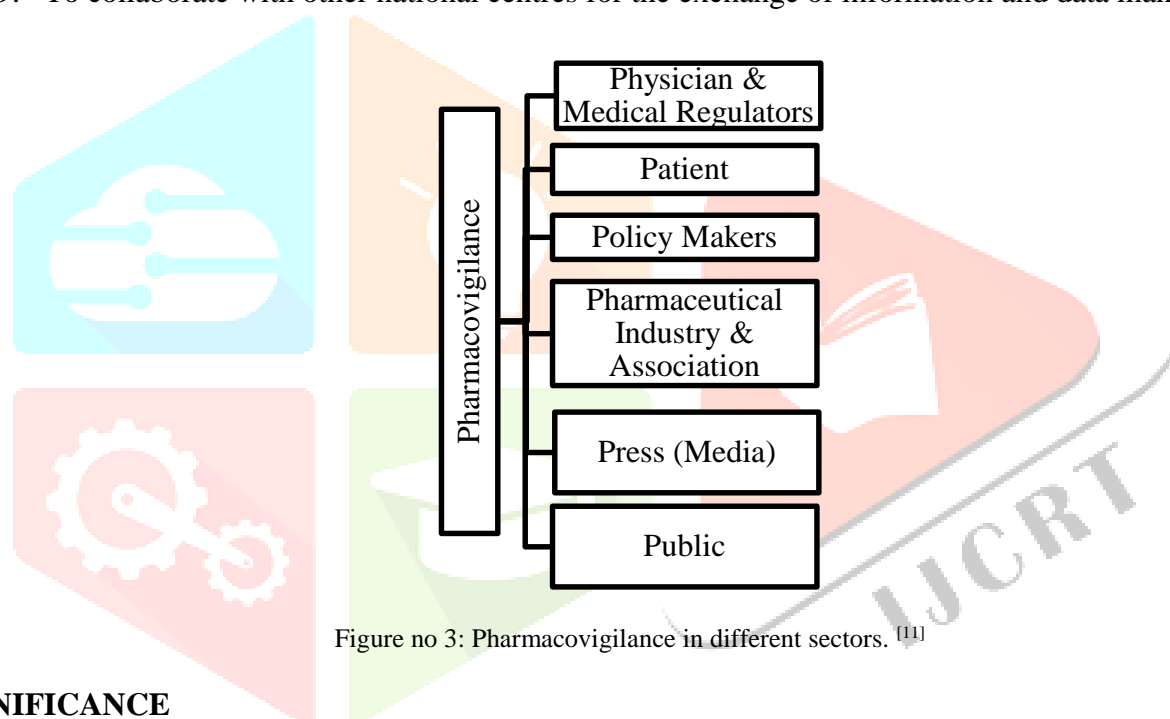


Figure no 3: Pharmacovigilance in different sectors. <sup>[11]</sup>

## SIGNIFICANCE

When a pharmaceutical drug is introduced in the market there are still a lot of things that are unknown about the safety of the new drug. To prevent all undue physical, mental and financial suffering of patients, pharmacovigilance proves to be an important monitoring system for the safety of medicines in a country with the support of doctors, pharmacists, nurses and other health professionals of the country.

The importance of pharmacovigilance is as follows:

- Safety monitoring of medicinal products
- Clinical trials
- Pharmacoepidemiological studies
- Developing case series

- Case reports
- Analysis of case series
- Use of data mining to identify product -event combination
- Spontaneous reporting <sup>[12]</sup>

## REPORTING AND FUNCTIONING

To fulfil the pharmacovigilance obligations for its marketed products as per regulations pharmaceutical company in India has to essentially carryout activities such as collection, included expedited reporting of serious unexpected adverse reaction and preparation.

A typical setup for phamacovigilance studies, people involved in various levels, organisational units and there function are given as below:

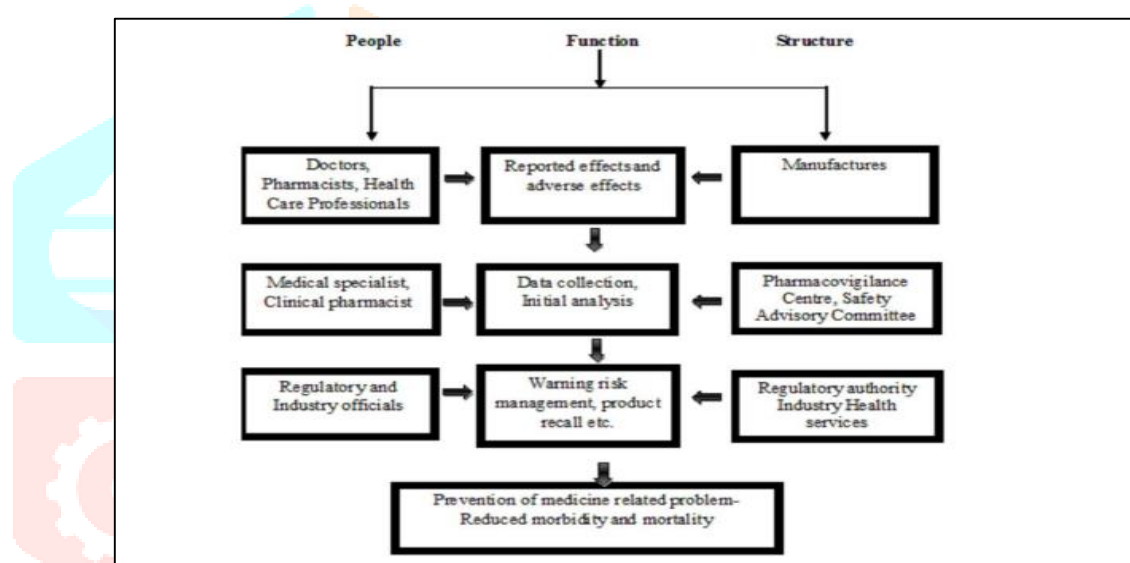


Figure no 4: A typical pharmacovigilance setup: people involved, functions and structure <sup>[11]</sup>.

## NEED

It is generally accepted that clinical development of medicines is a complex process which require huge amount of time for its completion. Necessary of pharmacovigilance arise which improve, it is dependable the timely observation of novel ADR of and patient sub group and introducing certain computed in sequence control the risk. It new and medically still developed treatment are evaluated for their effectiveness and protection under real life conditions after being marketed. Furthermore, more information is related to use in specific population group children and pregnant women and the old, about the efficacy protection of chronic use in mixture of drug. More adverse effect, risk factor, drug interaction have been the particular year of drug release is to be reported. <sup>[10]</sup>

## ROLE OF PHARMACIST IN PHARMACOVIGILANCE

- The commitment of the pharmacist to pharmacovigilance should, be that as it may, not be restricted to ADR announcing. <sup>[13]</sup>
- Assisting patients previous allergic status, patient's drug therapy, possible drug interaction.
- Pharmacists are associated with conveying social insurance offices and in addition proposing therapeutic staff on legitimate collection of medications.
- Along these lines, support of pharmacists in wellbeing the executive's framework is ending up extremely crucial step by step.
- Documentation of all suspected reported reactions.
- Educating the health care professionals about the importance of reporting an ADR.
- Pharmacovigilance information systems managed by pharmacist can recognised ADR in emerging countries where quality control of medicines is questionable.
- 73% of pharmacist work in hospital or pharmacy settings, where they can face events based on ADR or other drug related problems. Their involvement in pharmacovigilance system is crucial <sup>[14]</sup>.

## SCOPE OF PHARMACOVIGILANCE PROGRAMME OF INDIA:

- Before registration and selling of drugs within the country, its safety and efficaciousness expertise area unit primarily based totally on the employment of the drug in clinical trials. This trials in the main notice, ADR.
- Some vital reactions, like those, that take a protracted time to develop, or those, that occur seldom, might not be detected in clinical trials.
- So as to achieve a comprehensive safety profile of drugs, a continues post-marketing monitoring systems i.e. PV is crucial. So as to monitor the security of drugs, information from several source is employed for PV.
- This embrance spontaneous ADRs coverage mechanisms; medical literature published worldwide; action taken by regulative authorities in alternative countries.
- The aim of the pharmacovigilance programme of India is too, method and analysis it and use the inferences to advocate regulative interventions, besides human action risks to health care professionals and therefore the public. <sup>[4]</sup>

Table no 2: Activities currently included in the scope of pharmacovigilance <sup>[15]</sup>

Category	Specific Activities/Functions	Phase(s)*
Supporting patient safety during the conduct of clinical trials	Informed consent, institutional review board, data monitoring committee	1–4
Selecting the first safe dose; first-in-human	Preclinical data, especially PK/PD parameters	1
Establishing the safety profile	Assessing all phases of development, focusing on dose-limiting toxicity, maximum tolerated dose, AEs of special interest, on-target and off-target toxicities	1–4
Communicating information to stakeholders	Maintaining standard formats: Investigator's Brochure, Company Core Data Sheet, package insert, patient package insert, ClinicalTrials.gov	1–4
Attending to surveillance activities	Determining relationships between drugs and adverse events through passive and active methods	1–4
Monitoring safety-related issues that involve the quality of the manufactured product	Conducting health hazard assessments for manufacturing deviations, complaints	1–4
Managing risk: REMS, RMP	Understanding benefit–risk across patient populations and uses	1–4
Maintaining inspection readiness	Preparation for scheduled and unscheduled inspections of department activities	1–4
Training	Clinical investigators; internal customers throughout the company; vendors	1–4
Advertising and promotion review	Assuring consistency with important safety information	4
Providing medical information to health care professionals	Support for professional queries regarding product complaints, AE reports, product use	4
Conducting due diligence	Understanding critical safety information about products being considered for merger, acquisition, or licensing activities	1–4

AE = adverse event; PK/PD = pharmacokinetics/pharmacodynamics; REMS = Risk Evaluation and Mitigation Strategy; RMP = Risk Management Plan.  
\*The phase(s) of the drug development process that include the described activities.

## METHOD USED IN PHARMACOVIGILANCE

Many researcher developed different methods of causality assessment of ADRs by utilizing different criteria like chronologically relationship between the administration of the drug and the occurrence of the ADR, screening for non-drug related causes, confirmation of the reaction by in-vivo and in-vitro tests, and antecedent information of homogeneous events attributed to the suspect drug or to its therapeutic class, etc., to define ADRs in different categories. We would explicate them it in short as listed below.

1. Dangaumou's French method
2. Kramer et al. method
3. Balanced assessment method.
4. Naranjo et al. method (naranjo scale).

5. Loupi et al. method.
6. Ciba-Geigy method.
7. Roussel Uclaf causality assessment method.
8. Australian method. <sup>[16]</sup>

## **BASIC TERMINOLOGY USED IN PHARMACOVIGILANCE <sup>[1]</sup>**

### ➤ Adverse Drug Reaction (ADR)

Adverse drug reaction is a “response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of the physiologic function.” Adverse drug reaction can cause short term and long term hospitalisation and mortality.

### ➤ Adverse Drug Event (ADE)

Any untoward medical occurrence that may appear during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with the treatment.

### ➤ Difference between an ADE and ADR?

There may not be a causal relationship between a drug and an ADE, whereas, there is a causal link between a drug and an adverse drug reaction. Unexpected adverse reaction An adverse reaction, the nature or severity of which is not consistent with domestic labelling or market authorization or expected from characteristics of the drug.

### ➤ When do you consider an event to be serious?

If an event is associated with any one of the following, it is considered to be serious: death, life threatening, hospitalization or prolongation of hospitalization, congenital anomaly, disability, other: medically significant or important medical events.

### ➤ When do you consider a case to be medically confirmed?

A case is considered to be medically confirmed if it contains at least one event confirmed or reported by an HCP (health care professional). Note: HCP can be a physician, nurse, pharmacist, coroner or psychologist.

### ➤ What do you mean by causality?

In pharmacovigilance, causality assessment is a method of finding the relationship between drugs exposed and reported Adverse drug reactions (ADR). It includes, finding the temporal relationship between drugs and reported ADR, dechallenge, rechallenge, clinical and pathological characteristics of the events.



➤ Expectedness:

All AEs that are previously unobserved or undocumented are referred to as “unexpected,” (e.g., approved professional package insert or product label). Determination of expectedness is made by the sponsor on a case-by-case basis. Expected events typically do not require expedited reporting to the regulatory authorities.

➤ Relatedness

Relatedness is a term intended to indicate that a determination has been made that the event had a reasonable possibility of being related to exposure to the product. This assessment of causality may be based on factors such as biological plausibility, prior experience with the product, and temporal relationship between product exposure and onset of the event, as well as dechallenge (discontinuation of the product to determine if the AE resolves) and rechallenge (reintroduction of the product to determine if the AE recurs).

➤ Overdose

This refers to the administration of a quantity of a medicinal product given per administration or cumulatively, which is above the maximum recommended dose according to the authorized product information. Clinical judgement should always be applied.

➤ Off-label use

This relates to situations where the medicinal product is intentionally used for a medical purpose not in accordance with the terms of the marketing authorization.

➤ Misuse

This refers to situations where the medicinal product is intentionally and inappropriately used not in accordance with the terms of the marketing authorization.

➤ Abuse

This corresponds to the persistent or sporadic, intentional excessive use of a medicinal product, which is accompanied by harmful physical or psychological effects. 22 Occupational exposure This refers to the exposure to a medicinal product as a result of one’s professional or non-professional occupation. It does not include the exposure to one of the ingredients during the manufacturing process before the release as finished product.

➤ Medication error:

This is an unintended failure in the drug treatment process that leads to or has the potential to lead to harm to the patient.

- Lack of efficacy:

Unexpected failure of a drug to produce the intended effect as determined by previous scientific investigation.

- Dechallenge and rechallenge:

Challenge- in our pharmacovigilance world, this refers to the giving of the drug to the patient AE or treatment in question.

- Dechallenge

This refer to the stopping of the drug, usually after an adverse event (AE) or at the end of the planed treatment. Dechallenges may be complete or partial

- A positive dechallenge:

This refers to the AE disappearing after the stopping of the drug.

- Negative dechallenge:

This refers to AE not disappearing after the stoping of the drug

- Rechallenge:

This refers to the starting of the same drug after having stop it, usually for and AE. Rechallenges may also be complete or partial.

1. Positive rechallenge:

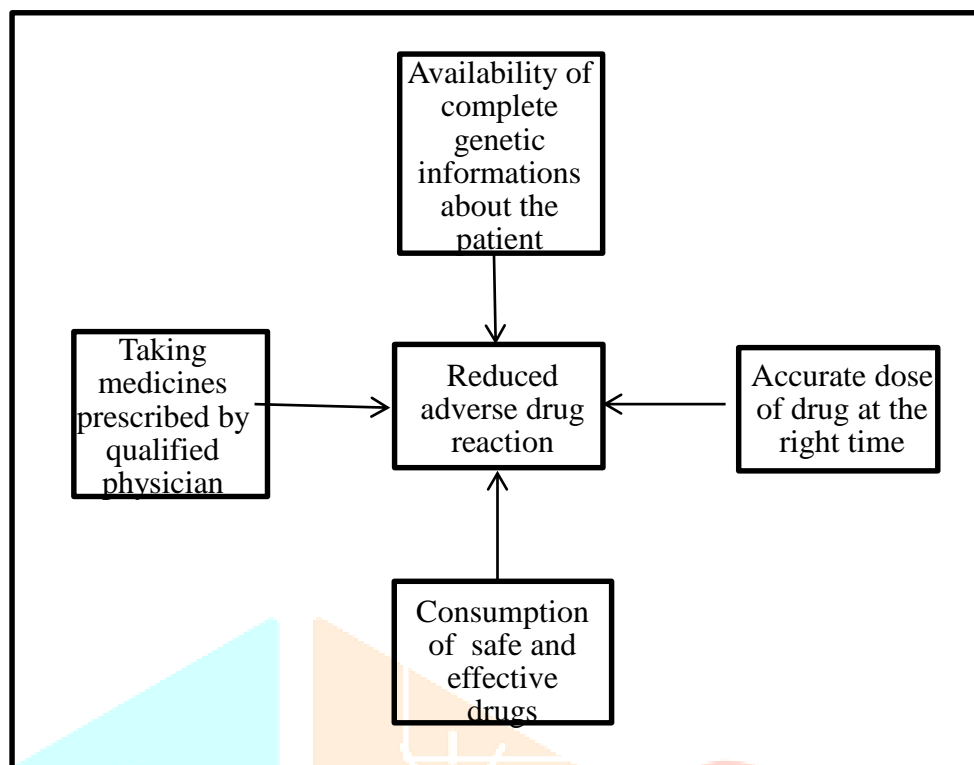
This refers to the AE requiring after starting the drug.

1. Negative rechallenge:

This is the case where the AE does not recure after the drug is restarted.

## FACTORS AFFECTING ON ADR: <sup>[17]</sup>

- Patient related factor:
  - Age
  - sex
  - Genetic influence
  - Concurrent disease ( renal, liver, cardiac )
  - Previous adverse drug reactions
  - Compliance with dosing regiment
  - Total number of medications
  - Misc. (diet, smocking, environmental exposure).

Figure no 5: Factors involve in ADR <sup>[18]</sup>

## BENEFITS OF ADR MONITORING

Many harmful adverse drug reaction resulting from medication used go undetected or unreported to regulatory authorities <sup>[19]</sup>. ADR not only add to the suffering to patient but also increase the morbidity and mortality with a financial burden on society <sup>[20]</sup>

An ADR monitoring and reporting program can furnish following benefits:

1. It caters information about quality and safety of pharmaceutical products.
2. It initiates risk management plans.
3. It prevents the predictable adverse effects and helps in measuring ADR adherence.
4. It instruct health care term i.e. patients, pharmacists and nurses about adverse drug effects and creates awareness ADRs.

The main objects and ADR monitoring is to disclose the quality and frequency of ADRs and to identify the risk factors that can cause the adverse reactions. <sup>[13]</sup>

➤ **TYPES OF ADRS** <sup>[21]</sup>

Type of reaction	Mechanism/Example
Type A (Augmented)	Predicted from the known pharmacology of the drug. These reactions are dose-dependent: examples are bleeding with anticoagulant
Type B (Bizarre)	Reactions are not predicted from the known pharmacology of the drug. They appear (but actually are not) relatively dose-independent, as very small doses might already elicit symptoms. They include immune-mediated side effect like maculopapular exanthema, but also other hypersensitivity reactions, like aspirin-induced asthma
Type C (Chemical/Chronic)	Which are related to the chemical structure and its metabolism e.g paracetamol hepatotoxicity.
Type D (Delayed)	Which appear after many years of treatment e.g. bladder carcinoma after treatment with cyclophosphamide
Type E (End of treatment)	Occur after drug withdrawal e.g. seizures after stopping phenytoin

**ADR REPORTING /ADVERSE EVENT REPORTING:** <sup>[6]</sup>

Reporting is the most commonly associated with Pharmacovigilance (PV) and consumes a considerable amount of resources of government agencies or drug regulatory authorities or drug safety departments in pharmaceutical organizations. Adverse Event (AE) reporting includes the receipt, triage, data maintaining, evaluation, distribution, reporting of AE data. The foundation of AE reports may include solicited reports from patient support programs, reports from clinical or post-marketing studies, spontaneous reports from healthcare professionals or patients or other intermediaries, reports from literature sources, reporting is a regulatory requirement in most countries, reports from the media including social media and websites and reports reported to drug regulatory authorities themselves. For pharmaceutical companies AE reporting also provides data that play an important in assessing the risk-benefit profile of a given drug.

The following are several elements of Adverse Event (AE) Reporting:

1. An identifiable patient
2. An identifiable reporter.
3. A suspect drug.
4. An adverse event.

## Suspected Adverse Drug Reaction Reporting Form

CDSCO Central Drugs Standard Control Organization Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India, FDA Bhavan, ITO, Kotla Road, New Delhi <a href="http://www.cdsc.org.in">www.cdsc.org.in</a>				AMC/NCC USE ONLY				
				AMC Report No.				
				Worldwide Unique No.				
A. Patient Information				12. Relevant tests/ Laboratory Data with dates				
1. Patient Initials	2. Date of birth.....	Sex: MF						
.....kgs		Weight						
B. Suspected Adverse Reaction				13. Other relevant history including pre-existing medical conditions (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/ renal dysfunction etc)				
5. Date of reaction stated (dd/mm/yyyy)								
6. Date of recovery (dd/mm/yyyy)								
7. Describe reaction or problem				14. Seriousness of the reaction				
				<input type="checkbox"/> Death (dd/mm/yyyy) _____ <input type="checkbox"/> Life threatening <input type="checkbox"/> Disability				
				15. Outcomes				
				Fatal                      Recovering                      Unknown Continuing                      Recovered                      Other.....				
C. Suspected medication(s)								
Sr. no.	Name	Manufacturer	Batch No.	Exp. Date	Dose use	Route use	Frequency	Reason
11. Concomitant medical product including self medication and herbal remedies with therapy dates (exclude those used to treat reaction)				D. Reporter				
				Name and Professional Address				
				.....				

Figure no 6: ADR reporting form <sup>[11]</sup>Table no 3: A list of some suspected and known drugs associated with adverse effect. <sup>[22]</sup>

Adverse Drug Reaction	Drugs
Phocomelia, Multiple Defects.	Thalidomide
Multiple Defects, Fetal death.	Methotrexate
Virilization of limbs, esophageal, cardiac defects.	Androgen
Virilization of female fetus	Progestin
Vaginal carcinoma in teenage female offspring.	Stilbesterols
Deformed teeth, retarded bone growth	Tetracycline
Various malformations	Phenytoin
ringing in ear	Quinidine
Neural tube defects	Carbamazepine
Growth retardation , nose, eye and hand defects	Warfarin
Low IQ baby, growth retardation	Alcohol
Orange colour urine	Rifampicine
Premature closer of ducts arteriosus	Indomethacin
Cleft palate, multiple defects	Anticancer drugs
Limb abnormalities, Spina bifida	Valproate sodium
Heart and CNS defects	Isotretenoin

## ❖ MORBIDITY AND MORTALITY OF ADR

Adverse drug reaction is ranked as one of the top tenth causes of morbidity and mortality in the developed world. Adverse drug reactions are documented in the USA to claim 1,00,000 to 2,18,000 lives annually are the third leading cause of death after heart disease and cancer. However, the burden of the problem may actually be underestimated, as in many instances, ADRs are not suspected, thereby leading to under-reporting.

Prior to approval, most drugs will only have been tested for short-term safety and efficacy limited number of carefully selected individuals. In some cases, as few as 500 subjects and seldom more than 5,000 will have received that drug prior to its release. In order to identify an ADR that occurs in 1 in 10,000 patients, at least 30,000 patients need to be treated with the drug.

Post approval monitoring facilitates observation of the drug profile for longer durations and for unapproved indication, effect of co-morbidities, co-administrations and the likely possibilities of non-compliance with drug administration instructions. [23]

## ❖ ESTABLISHING THE SAFETY PROFILE: [15]

In practice, an understanding of a new molecular entity's safety profile begins during animal studies. The pharmacokinetic/pharmacodynamics studies provide key insights into the first major group of adverse events expected to be seen during clinical development: the likely on-target adverse events that are usually seen in a dose-dependent fashion during dose-escalation studies.

The second major group of adverse events seen during development is the idiosyncratic, off-target event: it is generally uncommon, may be mild to severe, is rarely seen during animal studies, and the mechanism is usually unknown. Examples include drug-induced liver injury, hypoplastic/aplastic Anaemia.

## PHARMACOVIGILANCE IN INDIA

The national pharmacovigilance program established in January 2005, was to be overseen by the national pharmacovigilance advisory committee based in central drug standard control organisation (CDSCO). [24] India has more than half of a million qualified doctors and 15000 hospitals having a bed strength of 6, 24, 000. It is the fourth largest producer of pharmaceuticals in the world. It is emerging as an important trial hub in the world. Clearly aware of the enormity of task the Centralrug Standard Control Organization (CDSCO) has initiated a well structured and highly participative National pharmacovigilance program. It is largely based on the recommendations the WHO document titled "safety monitoring of medicinal products-guidelines for setting and running a pharmacovigilance centre". [12]

No. of individual case safety report <sup>[25]</sup>

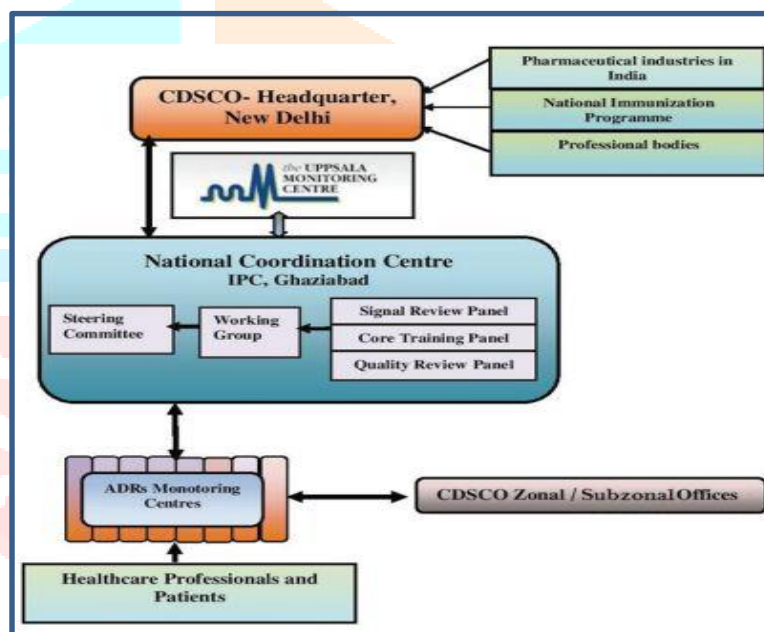
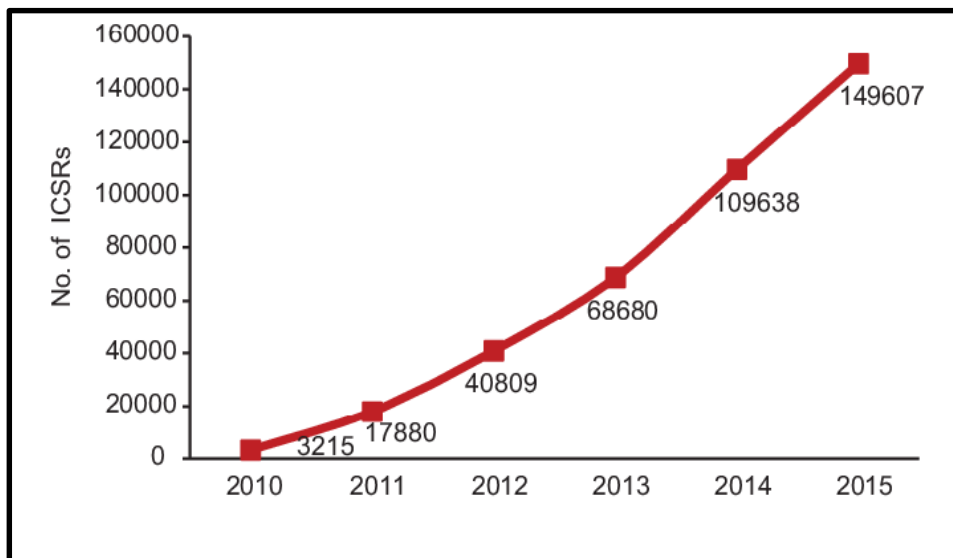


Figure no 7: PV in India <sup>[26]</sup>.

Table no 4: Role of various regulatory agencies. <sup>[11]</sup>

Agencies	Role of Agencies
Drug Controller General of India (DCGI)	Implementation the National Pharmacovigilance Program (NPP) in India.
Central Drugs Standard Control Organization (CDSCO)	Operate under the supervision of the National Pharmacovigilance Advisory Committee to recommend procedures and guidelines for regulatory interventions.
Department of Biotechnology	Provides product evaluation and validation through support for limited and large scale field trials for agriculture products and clinical trials for health care products.
Ministry of Environment & Forests (MOEF)	Project Advisory Committee approves guidelines for making data entries of the information provided by the environmental experts through the field trials for agriculture products and clinical trials for health care products.
Indian Council of Medical Research (ICMR)	Brought out the Policy Statement on Ethical Considerations involved in Research on Human Subjects in 1980 and revised these guidelines in 2000.

### ❖ REFERENCES:

- 1) Gawai PP, " Introduction and Evaluation of Pharmacovigilance for beginners", International Journal of Scientific Reports, September 2020, 6 (10), 425-432.
- 2) Jeetu G.,Anush G., " Pharmacovigilance: worldwide Master key for drug safety monitoring",General pharmacy, J. Younge pharm ,Vol 21,3.
- 3) Gupta N, Behmani K and Jangra A." Pharmacovigilance, International Classification of Disease and Adverse Reaction Reporting Tools used in the United States of America and Europe", Clinical practice, 2020, Vol-17(2), 1466-1477.
- 4) Nimesh S, Chaudhary A, Sharma A and Negi KD," Pharmacovigilance program of India: A review," ACTA Scientific Pharmaceutical Sciences, Vol- 3, issue 9, September 2019.
- 5) Muhammad Akhtar Abbas Khan, Saima Hamid, and Zaheer-Ud-Din Baber," PV in High- income countries: Current Developments and a Review of Literature, Pharmacy" 2023, 10-11.
- 6) Soni R, Kesari B ," A Review on Pharmacovigilance" , International Journal of Pharm Science Review and Research, 26 (2), May- June 2014, 237-241.
- 7) Singh S \*,Jaiprakash, Goyal N, Tomar R, Chaudhary A, "Review of Pharmacology" ,World Journal of Pharmacy and Pharm Science, 4 (6), 266-275.
- 8) Rajgopal J, Shilpi K, Srivastav AK," Pharmacovigilance: A review Article", Innovare Journal of medical Science, 4 (4), July 2016, 6-7.
- 9) Thobari J, D Pharm, PhD," Importance of Pharmacovigilance for Medicine" Gadjah MADA, University Yogyakarta, Indonesia , Adams CP, Brantner VV,(2010), Spending new drug development, Health Econ, 19:130-141 ( 2010).Clinical practice (2020 ), 17(2).1466-1477.
- 10) Rohilla A, Singh N, Kumar V, Sharma M , Dahiya A, Ashok Kushnoor, " Pharmacovigilance : Needs and objectives," Journal of Advanced Pharmacy Education and Research Oct- Dec 2012, 2 (4), 201-205.



- 11) Kumar S., Baldi A , " Pharmacovigilance in India: Perspective and Prospects", Journal of Drug Delivery and Therapeutics, 2013, 3(4), 237-246.
- 12) I. Lakshmi Anusha\*, M.Aashritha, K.Teja and R.Sridhar, "A Review of Pharmacovigilance and its important", World Journal of Pharmaceutical Sciences, 6 (1), 300-310.
- 13) Mohiuddin AK , " Pharmacovigilance: Present scenario and future goal," Indian journal of Pharmacy practice, Vol- 12, Issue 1, Jan- Mar 2019.
- 14)[[https://www.google.co.in/url?sa=i&url=https%3A%2F%2Fwww.slideshare.net%2Fframesh\\_2417%2Fpharmacovigilance-and-role-of-pharmacist&psig=AOvVaw3ZIK\\_q\\_aDY8PFgrk0BIhpY&ust=1679649017459000&source=images&cd=vfe&ved=0CAMQjB1qFwoTCPDZnsDa8f0CFQAAAAAdAAAAABAD](https://www.google.co.in/url?sa=i&url=https%3A%2F%2Fwww.slideshare.net%2Fframesh_2417%2Fpharmacovigilance-and-role-of-pharmacist&psig=AOvVaw3ZIK_q_aDY8PFgrk0BIhpY&ust=1679649017459000&source=images&cd=vfe&ved=0CAMQjB1qFwoTCPDZnsDa8f0CFQAAAAAdAAAAABAD)]
- 15) Beninger P, M D, MBA , "Pharmacovigilance: A overview," Clinical Therapeutics ,Vol- 40, Nov.2018,12.
- 16) Ahmed A M, Izham IM, Subish P," The Importance of the Consumer Pharmacovigilance System in Developing Countries: A case of Malaysia," Journal of Clinical and Diagnostic Research 2010, August,(4), 2929-2935.
- 17)[<https://www.google.co.in/url?sa=i&url=https%3A%2F%2Fwww.slideshare.net%2Fvirajshinde9659%2Fadverse-drug-reaction-83455149&psig=AOvVaw3ImpwBTpbuEDLdOXeTbsud&ust=1679384580169000&source=images&cd=vfe&ved=0CAMQjB1qFwoTCOiA3p-B6v0CFQAAAAAdAAAAABAD>]
- 18)[[https://www.google.co.in/url?sa=i&url=https%3A%2F%2Fwww.researchgate.net%2Ffigure%2Ffigure%2Ffactor-s-involved-in-adverse-drug-reactions-ADR\\_fig1\\_259382729&psig=AOvVaw3ImpwBTpbuEDLdOXeTbsud&ust=1679384580169000&source=images&cd=vfe&ved=0CAMQjB1qFwoTCOiA3p-B6v0CFQAAAAAdAAAAABAN](https://www.google.co.in/url?sa=i&url=https%3A%2F%2Fwww.researchgate.net%2Ffigure%2Ffigure%2Ffactor-s-involved-in-adverse-drug-reactions-ADR_fig1_259382729&psig=AOvVaw3ImpwBTpbuEDLdOXeTbsud&ust=1679384580169000&source=images&cd=vfe&ved=0CAMQjB1qFwoTCOiA3p-B6v0CFQAAAAAdAAAAABAN)]
- 19) Jorl Fossouo Tagne, B. Biomed, Reginal Amin Tokon, B Biomed , AACPA; Thu Ja Dang, Rachael Medonaid, Nilmini Wickramasinghe, Grad Dipmgst, " Reporting , Monitoring and handling of adverse drug reactions in Australia: Scoping Review", JMIR public health surveill 2023, Vol 9, 40080 .
- 20) Thobari J," Importance of Pharmacovigilance for Medicine" Gadjah MADA, University Yogyakarta, Indonesia , Adams CP, Brantner VV,(2010), Spending new drug development, Health Econ, 19:130-141 ( 2010).Clinical practice (2020 ), 17(2),1466-1477.
- 21) [<https://www.researchgate.net/profile/Zahra-Pourpak>]
- 22) Pawar S and Musal V," Pharmacovigilance: A Review," International Journal of Advanced Research, 8(01), 235-243.
- 23) Campbell JE, Williams MG, M. G.Lec, "A Review of Pharmacovigilance", West Indian Med J. 2014; 63(7):771.
- 24) Patil L, Patil S, Hubale S, Mane R, "Pharmacovigilance - A Review", International Journal of Scientific Research in Science and Technology, 1(3), 21.

25)[<https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.semanticscholar.org%2Fpaper%2FPharmacovigilance-Programme-of-India%253A-Recent-and-Kalaiselvan-Thota%2F5018295364c26498240e0bbb9466ff38ebe7bb84&psig=AOvVaw0QWwGBwdWLXJZham4ney-r&ust=1678952646570000&source=images&cd=vfe&ved=0CAMQjB1qFwoTCJCCjJK43f0CFQAAAAAdAAAAABAb>]

26)[<https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.mondaq.com%2Findia%2Fhealthcare%2F751258%2Findias-pharmacovigilance-regime&psig=AOvVaw0QWwGBwdWLXJZham4ney-r&ust=1678952646570000&source=images&cd=vfe&ved=0CAMQjB1qFwoTCJCCjJK43f0CFQAAAAAdAAAAABAk>].

