

**PHARMACOVIGILANCE PROGRAM OF INDIA- A STUDY**

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**ABSTRACT**

Indian Pharmaceutical market is evaluated around INR 90,000 crore INR and is being recognized worldwide as the 'Global pharmacy of Generic Drugs'. The domestic market of India is flooded with different types of medicines. This has led to the urgent need of establishing a competent body dedicated to the monitoring of the safety and efficacy of the products in the market. Due to these developments the Pharmacovigilance (PV) Program of India (PvPI) was set up in India. The primary goal of the organization as mentioned in the mission statement is to safeguard the health of the Indian population by ensuring that the benefits of use of medicine outweigh the risks associated with its use. This paper aims to analyze the PV program of India in detail and provide with a concise and up to date picture of the organization including its history, functioning and the challenges that its faces in terms of future considerations.

**KEYWORDS:** Pharmacovigilance, PvPI, Data Mining, Public health.

**INTRODUCTION**

The growth of clinical research industry around the globe has been unprecedented in the last few years. Innovations in the varied fields of science and technology, chemistry and physiology of human body coupled with better production techniques and improvement in logistics has lead to an explosion of drugs and other medical products in the market. The international developments have not failed to mirror in India as well. India, due to its rapid modernization and implementation of the open market policy has become one of the most sought out destinations of pharmaceutical companies around the globe.

The pharmaceutical industry in India is valued around INR 90,000 crore and is expected to have a growth rate of 12 – 14% per annum<sup>[1]</sup>, which is considerably above the current national average of 7 – 8%.<sup>[2]</sup> There is a 25% Compound Annual Growth Rate (CAGR) for exports in India currently.<sup>[3]</sup> The total pharmaceutical exports of India measure up to INR 40,000 crore. India is now being recognized as the 'Global pharmacy of Generic Drugs'. India has a distinction of providing generic quality drugs at affordable cost. The global focus on drug discovery and development is also shifting towards India. This can be inferred from the volume of applications received and processed by Central Drugs

Standard Control Organization (CDSCO), India. They have increased to 22,806 in 2009 from 10,000 in 2005.<sup>[3]</sup> This increase is also seen in New Drug Applications (NDA), Global Clinical Trials, Market authorization of Vaccine and Biotech products.

India being a huge country and home to the second largest population in the world (~ 1.3 billion) is a huge market for the pharmaceutical industry. It also raises the concern of safety. The Indian people are a highly diverse people in terms of ethnicity, disease prevalence patterns, practice of different systems of medicine, socioeconomic status etc and the effects of drugs and their side effects and adverse reactions are of prime concern. In order to address these issues, the Pharmacovigilance program was undertaken by the Government of India. The purpose of pharmacovigilance program in India is to collect, collate and analyze data to arrive at an inference to recommend regulatory interventions, besides communicating risks to healthcare professionals and the public.<sup>[3]</sup>

**RESEARCH METHODOLOGY**

Primary search was done using the PubMed, Google scholar and ResearchGate database till March 2016 and MeSH terms used were "Pharmacovigilance" and "India". Publications were limited to English language. Secondary hand search was conducted through the

cross-references of included articles. Relevant literature in common textbooks, bibliographies of papers, websites of relevant authorities including CDSCO, Ministry of Health and Family Welfare, Govt. of India, All India Institute of Medical Sciences (AIIMS), Public domain documentations from Knowledge Process Outsourcing (KPO) agencies such as Sciformix Technologies Pvt Ltd, Cognizant Technology Solutions India and review articles of suitable peer reviewed journals were analyzed for additional information.

## DEFINITIONS OF TERMS RELATED TO PHARMACOVIGILANCE

- 1) **Adverse Event:** An adverse event is defined as any untoward medical occurrence that may present during treatment with a drug but which does not necessarily have a relationship with its use.<sup>[4]</sup>
- 2) **Adverse drug reaction:** An adverse drug reaction (ADR) is any noxious, unintended and undesired effect of a drug, which occurs at a dose used in human for prophylaxis, diagnosis, therapy or modification of physiological function.<sup>[5]</sup>
- 3) **Post marketing surveillance:** Post-marketing surveillance (PMS) is the practice of monitoring the safety of a pharmaceutical drug or device after it has been released in the market.<sup>[6]</sup>
- 4) **Clinical trials:** Clinical trials are sets of tests in medical research and drug development that generate safety and efficacy data (or more specifically, information about adverse drug reactions and adverse effects of other treatments) for health interventions (e.g., drugs, diagnostics, devices, therapy protocols).<sup>[7]</sup>
- 5) **Safety signals:** Safety signal refer to a concern about an excess of adverse events compared to what would be expected to be associated with products use, which can arise from post marketing data and other sources, such as pre clinical data and events associated with other products in the same pharmacological class.<sup>[8]</sup>

## NATIONAL PHARMACOVIGILANCE PROGRAM

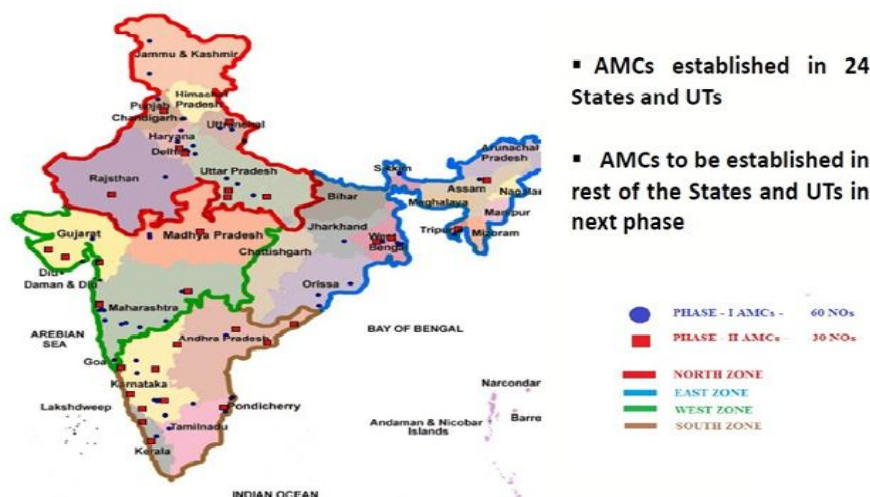
Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug related problems.<sup>[9]</sup> Pharmacovigilance is beneficial to everyone. It keeps the patients from harm's way, help the healthcare professionals and pharmaceutical industry to maintain their reputations and provides the regulatory authorities with data which is essential in formulation of policies. In India, Adverse Drug Reaction centers were established in 1980 by Indian Council of Medical Research (ICMR) and Drugs Controller General of India (DCGI) but their activities were limited to only a handful of institutions and the majority of the healthcare practitioners were unaware of these developments.<sup>[10,11]</sup> The Pharmacovigilance Programme of India (PvPI) was initiated by the Government of India in July 2010. All India Institute of Medical Sciences (AIIMS) was designated as the National Coordination Centre for monitoring Adverse Drug Reactions (ADRs) in the country. In the year 2010, 22 ADR monitoring centers including AIIMS, New Delhi was set up under this Programme. Later the National Coordination Centre was shifted from the All India Institute of Medical Sciences (AIIMS), New Delhi to the Indian Pharmacopoeia Commission, Ghaziabad, Uttar Pradesh on 15th April 2011.<sup>[12]</sup>

## MISSION

To safeguard the health of the Indian population by ensuring that the benefits of use of medicine outweigh the risks associated with its use.<sup>[13]</sup>

## VISION

To improve patient safety and welfare in Indian population by monitoring the drug safety and There by reducing the risk associated with use of medicines.<sup>[13]</sup>



**Fig 1: Adverse Event Monitoring Centers in India**

Adapted from Pharmacovigilance Programme of India (PvPI), Indian Pharmacopoeia Commission, 2013.

**OBJECTIVES**<sup>[13,14]</sup>

- To monitor Adverse Drug Reactions in Indian population
- To create awareness amongst health care professionals about the importance of ADR reporting in India
- To monitor benefit-risk profile of medicines
- Generate independent, evidence based recommendations on the safety of medicines
- Support the CDSCO for formulating safety related regulatory decisions for medicines
- Communicate findings with all key stakeholders
- Create a national centre of excellence at par with global drug safety monitoring standards

**CURRENT SCENARIO**

Globally, various organizations and government authorities have databases which are large enough to undertake data mining activities with regard to the adverse events relating to pharmaceutical products. The United States Food and Drug Administration (USFDA) database has 100,000+ adverse drug reactions and WHO safety database is much bigger than the USFDA database. The increase in the awareness among Indian health care providers regarding Pharmacovigilance processes has led to an increase in the amount of data in the Indian databases. Thus, with the addition of more and more data and the sharing and comparison with international databases such as USFDA, WHO and

Uppsala Monitoring Center (UMC) CDSCO will be able to take decisions based on its own data obtained from the Indian population thereby making significant contribution in the field of pharmacovigilance worldwide.<sup>[12]</sup>

Various steps have been undertaken in the national level to increase the data collection regarding ADR/ AE in the country by increasing the awareness among health care professionals. In order to arrive at a meaningful conclusion, on any safety issue regarding medications, data is of at most importance. The sample size of the database plays the most important role in this regard. The relevance of the conclusion is directly proportional to the sample size of in the database. Thus it can be safely said that the various medical colleges in India, both public and private would be the cornerstone to the pharmacovigilance programme of India. Depending on the already established private practitioners as the primary source of data would not yield much results as they wouldn't be much eager to alter their already set methods of practicing. The various medical collages would act as the peripheral ADR monitoring centers, collecting and maintaining the ADR reports, undertaking follow ups whenever deemed necessary as per the standard operating procedures, entering and maintaining the data in the prescribed database software (Vigiflow) and reporting to the National Coordinating Center.<sup>[12]</sup>

**SUSPECTED ADVERSE DRUG REACTION REPORTING FORM**

For VOLUNTARY reporting of Adverse Drug Reactions by healthcare professionals

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 www.cdsc0.nic.in										(AMC/ NCC Use only) AMC Report No. _____ Worldwide Unique no. _____									
<b>A. Patient Information</b>					12. Relevant tests / laboratory data with dates														
1. Patient Initials _____		2. Age at time of Event or date of birth _____		3. Sex <input type="checkbox"/> M <input type="checkbox"/> F		4. Weight _____ Kgs													
<b>B. Suspected Adverse Reaction</b>					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) _____					14. Seriousness of the reaction														
6. Date of recovery (dd/mm/yyyy) _____					<input type="checkbox"/> Death (dd/mm/yyyy) _____ <input type="checkbox"/> Life threatening _____ <input type="checkbox"/> Hospitalization-initial or prolonged _____ <input type="checkbox"/> Disability _____														
7. Describe reaction or problem _____					<input type="checkbox"/> Congenital anomaly <input type="checkbox"/> Required intervention to prevent permanent impairment / damage <input type="checkbox"/> Other (specify) _____														
15. Outcomes					<input type="checkbox"/> Fatal <input type="checkbox"/> Recovering <input type="checkbox"/> Continuing <input type="checkbox"/> Recovered <input type="checkbox"/> Unknown <input type="checkbox"/> Other (specify) _____														
<b>C. Suspected medication(s)</b>																			
S.No	8. Name (brand and /or generic name)	Manufacturer (if known)	Batch No./ Lot No. (if known)	Exp. Date (if known)	Dose used	Route used	Frequency	Therapy dates (if known give duration)		Reason for use of prescribed for									
i.								Date started	Date stopped										
ii.																			
iii.																			
iv.																			
9. Reaction abated after drug stopped or dose reduced		10. Reaction reappeared after reintroduction																	
Yes		No		Unknown		NA		Reduced dose		Yes		No		Unknown		NA		If reintroduced dose	
i.		ii.		iii.		iv.													
11. Concomitant medical product including self medication and herbal remedies with therapy dates (exclude those used to treat reaction)										<b>D. Reporter (see confidentiality section in first page)</b>									
										16. Name and Professional Address : _____									
										Pin code : _____ E-mail : _____									
										Tel. No. (with STD code): _____									
										Occupation : _____ Signature : _____									
										17. Causality Assessment									
										18. Date of this report (dd/mm/yyyy)									

Fig2: ADR Reporting Form (PvPI)

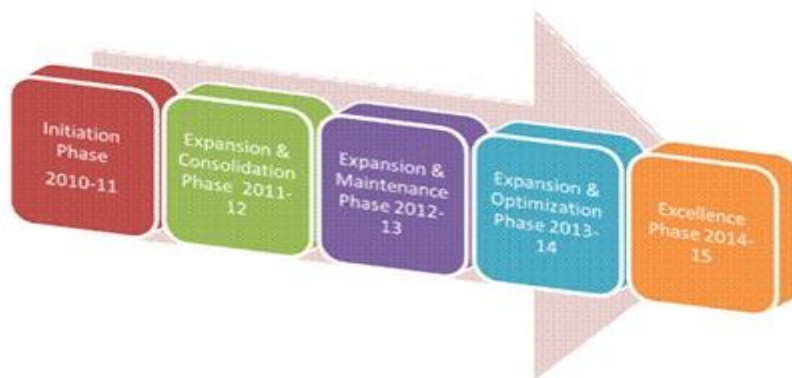
## ORGANISATION OF INDIAN PHARMACOVIGILANCE SYSTEM

The program is coordinated by Indian Pharmacopoeia Commission (IPC) Gaziabad, as NCC under steering committee. The Drug Controller General of India (GCI) is the chairman of the eight member steering committee. The Officer-in-charge (New Drugs), CDSCO, New Delhi is the member secretary. Steering Committee and Strategic Advisory Committee along with Core Training Panel and Quality Review Panel monitor and administer the deployment of the program. In the PvPI, there is effective communication channels among the major players to make sure that there is continuous bidirectional and productive data and knowledge transfer.

## PROGRAM ROADMAP FOR PvPI

1. Initiation Phase 2010-11
2. Expansion and consolidation phase 2011-12
3. Expansion and Maintenance Phase 2012-13
4. Expansion and Optimization Phase 2013-14
5. Excellence Phase 2014-15

PvPI has presently entered the excellence phase and is striving to serve the population of India through private – public partnership as well as cooperation with international regulatory authorities. The aim of the initiative currently is to provide a much safer public health through the use of technology and tools such as data mining.



**Fig3: Program Roadmap (PvPI)**

*Adapted from Pharmacovigilance Programme of India (PvPI), Indian Pharmacopoeia Commission, 2013.*

## HIERARCHY OF PHARMACOVIGILANCE CENTERS UNDER PvPI

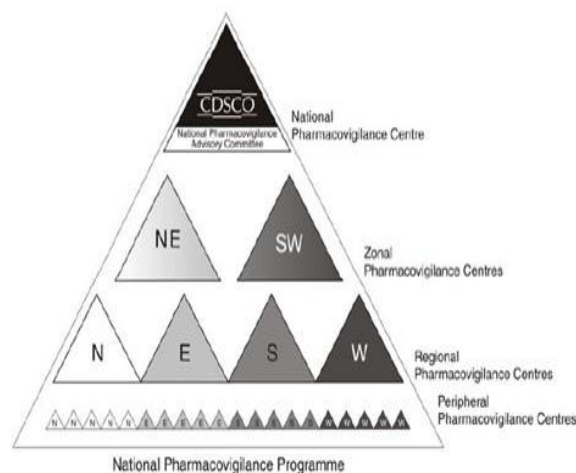
The PvPI has a four tier configuration.<sup>[15]</sup>

1. National Pharmacovigilance Center
2. Zonal Pharmacovigilance Center
3. Regional Pharmacovigilance Center
4. Peripheral Pharmacovigilance Center

The teaching and non-teaching hospitals, clinics and pharmacies in each state and union territory includes the Peripheral Pharmacovigilance centers. Each Peripheral Pharmacovigilance Center records and forwards ADR information to its respective Regional Pharmacovigilance Center weekly. There are five regions for regional PV centers North, East, Central, West and South.

The Regional Pharmacovigilance Centers report to the Zonal Pharmacovigilance Centers after assessment of causality of the reported event/reaction. There are two Zonal Pharmacovigilance Centers in India, one at KEM Hospital, Mumbai and the other at All India Institute of Medical Sciences, New Delhi. They also undertake the basic activities of PV such as data collection and analysis pertaining to ADR/AE. They report to the National Pharmacovigilance center and also undertake specific projects on the recommendations of the later.

The National Pharmacovigilance Center recommends to the Central Drugs Standard Control Organization regarding actions required based on the analysis of the ADR data generated in the country and Periodic Safety Update Reports (PSUR) submitted by pharmaceutical companies. They are also responsible for the dissemination of the data regarding ADR within the country as well as sharing the data with various international organizations and regulatory bodies such as the WHO and US FDA.



**Fig 4: Hierarchy of PV Centers under PvPI**



Adapted from National Pharmacovigilance Protocol, Ministry of Health and Family Welfare, Govt. of India.

### INTERNATIONAL COLLABORATIONS

PvPI collaborates with multiple international organizations and authorities in its pharmacovigilance efforts. The main collaboration is with the following organizations.<sup>[17]</sup>

1. World Health Organization (WHO)
2. Uppsala Monitoring Center (UMC), Sweden
3. The Council for International Organizations of Medical Sciences (CIOMS)

The WHO's International Drug Monitoring Program is based on the principle of data sharing by the member states. Currently there are more than 100 countries participating in the program. UMC is the field name for the WHO Collaborating center for International Drug Monitoring. The collection, assessment and communication of information from member countries are carried out by the UMC.<sup>[16]</sup> The CIOMS is a globally – oriented think tank that provide guidance on drug safety issues. CIOMS is a subsidiary of WHO and its reports are used in formulating policies by the WHO.

#### WHO-UMC Completeness Scoring for Indian ICSRs

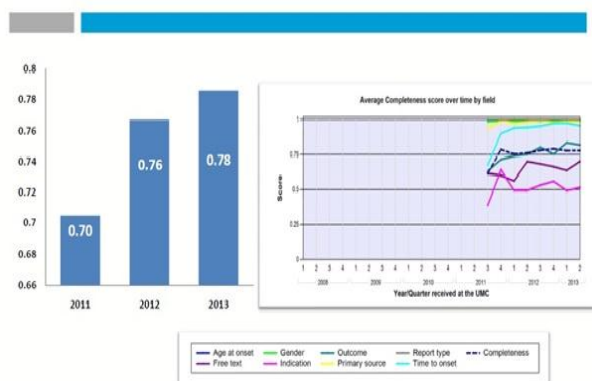


Fig 5: WHO UMC Completeness Scoring for Indian ICSRs

Adapted from Pharmacovigilance Programme of India (PvPI), Indian Pharmacopoeia Commission, 2013.

### FUTURE CONSIDERATIONS

- Involving professional organizations of healthcare professionals to educate their members about the program leading to a sustainable participation.
- Using new communication methods such as email and social media to tap into the patient pool for more effective data aggregation.
- Clearing the legal barriers such as the problem of data privacy while reporting a case, which will in turn increase the volume of reported cases.
- Address the issue of data ownership and data theft issues so as to make case reporting hassle free.

- Increasing the scope of PvPI to that of traditional medicine and treatment modalities such as Ayurveda, Homeopathy and Unani etc.<sup>[18]</sup>
- Increased focus on drug safety issue on vulnerable population such as children, elderly and pregnant women.
- Create a framework for ADR reporting for alternate medications such as homeopathy, ayurveda etc.
- Incorporate data collection on immunization via public health authorities.
- Develop infrastructure (computers, internet connectivity etc) so that there is maximum reporting and usher in an era of complete reporting.

### CONCLUSION

Even though the concept of pharmacovigilance was present in India from 1980s, unfortunately it was not accessible to everyone and was limited to certain institutions. Because of this it can be said truly that Pharmacovigilance industry in India is still at its infancy. However, there has been a continuous growth in this field from 2009 and an exponential growth especially from 2012. This trend is due to the rapid growth in the economy, public-private partnerships, policies of regulatory authorities and above all the general awareness of the healthcare practitioners as well as general public. Even though the trend is positive, there are many hurdles to be passed. The field is set. The tools are in place. Now the success of the Industry will depend on the persistence and sustainability with which we execute our business and strive for excellence in the international arena.

### REFERENCES

1. "Pharmacovigilance: The Present Status And Future Prospects In India." Pharma Tutor. Accessed March 17, 2016. <http://www.pharmatutor.org/articles/pharmacovigilance-present-status-future-prospects-india>.
2. "Economy of India." Wikipedia. Accessed March 17, 2016. [https://en.wikipedia.org/wiki/Economy\\_of\\_India](https://en.wikipedia.org/wiki/Economy_of_India).
3. "Pharmacovigilance Programme of India (PvPI) for Assuring Drug Safety." Aiims.edu. Accessed March 17, 2016. <http://www.aiims.edu/aiims/departments/pharmacology/pvpi/pvmainfram.htm>.
4. Nebeker R, Barach P, Clarifying adverse drug events: A clinician's guide to terminology, documentation, and reporting, *Ann Intern Med*, 2004; 2: 482-576.
5. Prakash S, Pharmacovigilance in India, *Indian J Pharmacol*, 2007; 1: 125-128.
6. Phillips KA, Veenstra DL, Oren E, Potential role of pharmacogenomics in reducing adverse drug reactions: A systematic review, *JAMA*, 2001; 4: 2270-2279.
7. Weinshilboum R, Inheritance and drug response, *N Engl J Med*, 2003; 6: 529-537.

8. DeVane CL, Clinical significance of drug binding, protein binding and binding displacement drug interactions, *Psychopharmacol Bull*, 2002; 2: 5-21.
9. World Health Organization Collaborating Center for International Drug Monitoring. The importance of pharmacovigilance. Safety monitoring of medicinal products. Geneva: World Health Organization, 2002.
10. Kshirsagar NA, Karande S, Potkar CN. Adverse drug reaction monitoring in India. *J Assoc Physicians India*, 1993; 41: 474-476.
11. Gogtay NJ, Dalvi SS, Kshirsagar NA. Safety monitoring: An Indian Perspective. *Int J Risk Safety Med*, 2003; 16: 21-30.
12. Kalaiselvam, K., Dr. *Pharmacovigilance Programme of India (PvPI)*. New Delhi: Indian Pharmacopoeia Commission, 2013.
13. "Mission-Vision-Objectives." PVPI. Accessed March 17, 2016. [http://www.ipc.gov.in/PvPI/pv\\_about.html](http://www.ipc.gov.in/PvPI/pv_about.html).
14. Rehan, Harmeet Singh. "Status of Pharmacovigilance Program in India." *Tamil Nadu Journal of Veterinary and Animal Sciences* 9, no. 6 (December 2013): 417-20. Accessed March 02, 2016.
15. Govt. of India. Ministry of Health and Family Welfare. "National Pharmacovigilance Protocol."
16. Jonas H, Philosophical reflections on experimenting with human subjects, *Daedalus*, 1969; 98: 219-247.
17. Baldi, Ashish and Sumit Kumar. "Pharmacovigilance in India: Perspectives and Prospects." *Journal of Drug Delivery and Therapeutics*, 2013; 3(4): 237-43.
18. Protocol National Pharmacovigilance Programme for Ayurveda, Siddha and Unani (ASU) Drugs. Sponsored by Department of AYUSH, Ministry of Health & Family Welfare, Government of India, New Delhi.