Pharmacovigilance Programme of India

1. Introduction

1.1 The Indian Pharmacopoeia Commission

Indian Pharmacopoeia Commission (IPC) is an autonomous institution of the Ministry of Health and Family Welfare which sets standards for all drugs that are manufactured, sold and consumed in India. IPC is created to set standards of drugs in the country. Its basic function is to update regularly the standards of drugs commonly required for treatment of diseases prevailing in this region. It publishes official documents for improving Quality of Medicines by way of adding new and updating existing monographs in the form of Indian Pharmacopoeia (IP). It further promotes rational use of generic medicines by publishing National Formulary of India.

The Pharmacovigilance effort in the India is coordinated by The Indian Pharmacopoeia Commission and conducted by the Central Drugs Standard Control Organization (CDSCO). The main responsibility of the IPC is to maintain and develop the Pharmacovigilance database consisting of all suspected serious adverse reactions to medicines observed.

Indian Pharmacopoeia Commission (IPC) is functioning as a National Coordination Centre (NCC) for Pharmacovigilance Programme of India (PvPI). NCC is operating under the supervision of steering committee which recommends procedures and guidelines for regulatory interventions. The main responsibility of NCC is to monitor all the adverse reactions of medicines being observed in the Indian population and to develop and maintain its own pharmacovigilance database.

The aim of the commission that acts like the National Coordinating Centre (NCC) for PvPI is for safety of the patient, safety of the population with respect to use of the Drug.

The Govt. of India have created a separate, dedicated, autonomous institution in the form of the Indian Pharmacopoeia Commission (IPC) to deal with matters relating to timely publication of the Indian Pharmacopoeia which is the official book of standards for drug included therein, in terms of the Second Schedule to the Drugs and Cosmetics Act, 1940 so as to specify the standards of identify, purity and strength of the drugs imported, manufactured for sale, stocked or exhibited for sale or distributed in India.

The mandate of the Commission is to perform, inter-alia, functions such as revision and publication of the Indian Pharmacopoeia and National Formulary of India on a regular basis besides providing IP Reference Substances and training to the stakeholders on
Pharmacopoeial issues. The Commission has become fully operational from 1st January, 2009 as an Autonomous Body, fully financed by the Central Government with specific budgetary allocations under administrative control of the Ministry of Health and Family Welfare. The Secretary, Ministry of Health and Family Welfare, is the Chairperson and the Chairman-Scientific Body is the Co-Chairman of the Commission. The Secretary-cum-Scientific Director is the Chief Scientific and Executive Officer of the Commission.

1.2 Pharmacovigilance Programme of India (PvPI)

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 collaboration with Indian Pharmacopeia commission, Ghaziabad is initiating a nation-wide Pharmacovigilance Programme for protecting the health of the patients by assuring drug safety. The Programme shall be coordinated by the Indian Pharmacopeia commission, Ghaziabad as a National Coordinating Centre (NCC). The centre will operate under the supervision of a Steering Committee.

1.2.1 Background

The Pharmacovigilance Programme of India (PvPI) was initiated by the Government of India on 14th July 2010 with the All India Institute of Medical Sciences (AIIMS), New Delhi as the National Coordination Centre for monitoring Adverse Drug Reactions (ADRs) in the country for safe-guarding Public Health. In the year 2010, 22 ADR monitoring centres including AIIMS, New Delhi was set up under this Programme. To ensure implementation of this programme in a more effective way, 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.

1.2.2 Scope

Before registration and marketing of medicine in the country, its safety and efficacy experience is based primarily on the use of the medicine in clinical trials. These trials mainly detect common adverse reactions. Some important reactions, such as those, which take a long time to develop, or those, which occur rarely, may not be detected in clinical trials. In addition, the controlled conditions under which medicines are used in clinical trials do not necessarily reflect the way they will be used in practice. For a medicine to be considered safe, its expected benefits should be greater than any associated risks of harmful reactions. So in order to gain a comprehensive safety profile of medicine, a continuous post-marketing
monitoring system i.e. Pharmacovigilance is essential. In order to monitor the safety of medicine, information from many sources is used for pharmacovigilance. These include spontaneous (ADRs) reporting mechanism; medical literature published worldwide, action taken by regulatory authorities in other countries, etc. Since there exist considerable social and economic consequences of adverse drug reactions and the positive benefit/cost ratio of implementing appropriate risk management - there is a need to engage healthcare professionals and the public at large, in a well structured programme to build synergies for monitoring adverse drug reactions in the country.

The purpose of the PvPI is to collate data, process and analyze it and use the inferences to recommend regulatory interventions, besides communicating risks to healthcare professionals and the public.

1.2.3 International Scenario

Globally, the size of the database for pharmacovigilance in developed countries are big enough to perform data mining and to check if any drug has been found to be causally associated with and significantly responsible for any serious and hitherto unknown side effects. For example, the USFDA database has 100,000 adverse drug reactions; similarly WHO safety database is several times bigger than the USFDA database. With the increasing awareness amongst the healthcare professionals in India, the Pharmacovigilance data under PvPI is being continuously increasing. Thus, with the addition of more and more data, 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.

1.2.4 National Scenario

Several steps have been taken to increase the awareness amongst the health care professionals in India under this programme and therefore collect more data. Arriving at a meaningful conclusion on safety issue of medicines on the basis of the analysis of ADRs in the pharmacological database depends on the sample size of the database. The larger is the data for any drug, the higher will be the likelihood of saying with confidence that the conclusions or inferences being drawn from that data are meaningful and significant. Therefore, if an analysis is performed on a very small sample size the likelihood of any conclusion or inferences being drawn from that data decreases substantially. The Indian data includes adverse reactions from a large number of drugs and includes non serious adverse drug reactions data also besides the serious side effect data. The Medical Colleges (both
Government & Private) are the corner stone of the Pharmacovigilance Programme of India. They act as peripheral Adverse Drug Reaction Monitoring Centres (AMCs) which are responsible for collecting the ADRs, performing the follow up with the patient to check completeness of the ADRs as per Standard Operating Procedures (SOPs) and to enter the Data in the prescribed software (VigiFlow) to report to NCC.

1.2.4.1 Committee under PvPI

The programme is administered and monitored by

- Steering Committee

1.2.4.2 Collection of ADRs reports

- MCI approved medical colleges and hospitals
- Private hospital
- Public health programmes
- Autonomous Institutions (ICMR etc)

1.3 Mission

Safeguard the health of the Indian population by ensuring that the benefits of use of medicine outweigh the risks associated with its use.

1.4 Vision

To improve patient safety and welfare in Indian population by monitoring the drug safety and thereby reducing the risk associated with use of medicines.

1.5 Objectives

- To create a nation-wide system for patient safety reporting
- To identify and analyse the new signal (ADR) from the reported cases
- To analyse the benefit - risk ratio of marketed medications
- To generate the evidence based information on safety of medicines
- To support regulatory agencies in the decision-making process on use of medications
- To communicate the safety information on use of medicines to various stakeholders to minimise the risk
- To emerge as a national centre of excellence for pharmacovigilance activities
- To collaborate with other national centres for the exchange of information and data management
To provide training and consultancy support to other national pharmacovigilance centres located across globe

1.6 Implementation of PvPI

IPC understood the need for establishing local hospital based centres across the nation for the better patient safety. It was important to monitor both the known and hitherto unknown side effects of medicines in order to determine any new information available in relation to their safety profile. In a vast country like India with a population of over 1.2 billion and with vast ethnic variability, different disease prevalence patterns, practice of different systems of medicines, different socioeconomic status, it was important to have a standardized and robust pharmacovigilance and drug safety monitoring programme for the nation.

1.6.1 Short term goals

- To develop and implement pharmacovigilance system in India
- To enrol, initially, all MCI approved medical colleges in the program covering north, south, east and west of India
- To encourage healthcare professionals in reporting of adverse reaction to drugs, vaccines, medical devices and biological products
- Collection of case reports and data

1.6.2 Long term goals

- To expand the pharmacovigilance programme to all hospitals (govt. & private) and centers of public health programs located across India
- To develop and implement electronic reporting system (e-reporting)
- To develop reporting culture amongst healthcare professionals
- To make ADR reporting mandatory for healthcare professionals

1.7 Collaboration with World Health Organization (WHO) - Uppsala Monitoring Centre (UMC)

WHO and UMC work with and/or provide technical support to more than 130 countries worldwide. The long term objective of the PvPI is to establish a ‘Centre of Excellence’ for Pharmacovigilance in India. To achieve this objective, the PvPI National Coordinating Centre will collaborate with the World Health Organization (WHO) - Uppsala Monitoring Centre (UMC) based in Sweden. The responsibilities of WHO-UMC towards NCC are as follows:
- Training of the staff at the PvPI national coordinating centre at IPC Ghaziabad, the ADRs Monitoring centers in medical colleges across the country.
- Usage of UMC’s Vigiflow software (for medicines) at no cost to PvPI.
- Access to Vigi-base, which contains worldwide medicines safety data
- Access to early information about potential safety hazards of medicines (worldwide data)
- Technical collaboration for PvPI.
- Technical collaboration for a regular publication that will be issued by the PvPI NCC for distribution to the ADR Monitoring centers and other stakeholders.
- CDSCO Headquarters has held several meetings with UMC over the past few years to discuss the potential role and approach for technical collaboration.

1.7.1 WHO - UMC & INDIA

The WHO Program for International Drug Monitoring provides a forum for WHO member states that includes India to collaborate in the monitoring of drug safety. Within the Program, individual case reports of suspected adverse drug reactions are collected and stored in a common database, presently containing over 3.7 million case reports.

Since 1978, the Uppsala Monitoring Centre (UMC) in Sweden has carried out the Program. The Uppsala Monitoring Centre is responsible for the collection of data about adverse drug reactions from around the world, especially from countries that are members of the WHO including India. Member countries send their reports to the Uppsala Monitoring Centre where they are processed, evaluated and entered into the WHO International Database. When there are several reports of adverse reactions to a particular drug this process may lead to the detection of a signal – an alert about a possible hazard communicated to member countries. This happens only after detailed evaluation & expert review.

These ADR reports are assessed locally and may lead to action within the country. Through membership of The WHO International Drug Monitoring Program, a country can know if similar reports are being made elsewhere. (The European Union also has its own scheme.) India is a country with a large patient pool and healthcare professionals, yet ADR reporting is in its infancy.
### 2. Responsibilities of the stakeholders in the Programme

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<th>Functions of the Stakeholders</th>
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<tr>
<td><strong>ADRs Monitoring Centre</strong></td>
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<tr>
<td>• Collection of ADR reports</td>
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<td>• Perform follow up with the complainant to check completeness as per SOPs</td>
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<td>• Data entry into Vigiflow</td>
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<td>• Reporting to PvPI National Coordinating Centre (PvPI NCC) through Vigiflow with the source data (original) attached with each ADR case</td>
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<td>• Training/ sensitization/ feedback to physicians through newsletters circulated by the PvPI NCC</td>
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| **PvPI ADR Monitoring Centre other than medical colleges [Corporate hospitals, autonomous institutes, Pharmaceutical industry, public health Programmers ]** |
| • Collection of ADR reports |
| • Perform follow up with the complainant to check |
| • completeness as per SOPs |
| • Report the data to CDSCO HQ |

| **(PvPI NCC, IPC Ghaziabad)** |
| • Preparation of SOPs, guidance documents & training manuals |
| • Data collation, Cross-check completeness, Causality Assessment etc as per SOPs |
| • Conduct Training workshops of all enrolled centers |
| • Publication of Medicines Safety Newsletter |
| • Reporting to CDSCO Headquarters |
| • Analysis of the PMS, PSUR, AEFI data received from CDSCO HQ |

| **ZONAL/Sub-zonal CDSCO Offices** |
| • Provide procurement, financial and administrative support to ADR monitoring centers |
| • Report to CDSCO HQ |

| **CDSCO, HQ, New Delhi** |
| • Take appropriate regulatory decision & actions on the basis of recommendations of PvPI NCC at IPC Ghaziabad. |
| • Propagation of medicine safety related decisions to stakeholders |
| • Collaboration with WHO-Uppsala Monitoring Center - Sweden |
| • Provide for budgetary provisions & administrative support to run PvPI |
2.1 **Roles & Responsibilities of PvPI Personnel at ADR Monitoring Centre (AMC)**

1. At PVPI - AMC, the designated Centre Coordinator is responsible for the proper functioning of AMC. In absence of the coordinator, the designated Sub-coordinator is responsible for the smooth functioning of the centre.

2. The Technical Associate appointed by NCC will be responsible for the collection and follow up of ADRs, which have to be reported to the AMC coordinator, all the scrutinized and signed ADR reports should be entered in Vigi-Flow by technical associate. Every report has to be sent to the central assessment at NCC.

3. Collection, checking completeness for a valid case, causality assessment and scrutinizing the ADR reports received will be done as per SOPs by Centre Coordinator/ Sub-Coordinator.

4. The centre coordinator is responsible for sending the monthly reports of their AMC to NCC.

5. Sensitization of the physicians/ healthcare professionals/ students/ patients of the hospitals for spontaneous ADRs reporting by various modes (lectures on ADR reporting, email, telephone, pamphlet and newsletter) should be undertaken by the centre coordinator.

6. Feedback to all healthcare professionals involved in reporting, should be sent by the AMC Centre Coordinators.

2.2 **Roles & Responsibilities of PvPI Personnel at National Coordinating Centre (NCC)**

1. The NCC personnel will be responsible for review completeness of ADR reports, to perform quality checks, causality assessment and commit ADR reports sent by AMC to WHO-UMC.

2. Monitoring of number of ADR reports entered in Vigi-Flow by AMCs and the Day-To-day Activity Report (DTAR) will be sent to them on weekly basis.

3. Cumulative Centre wise Status Report (CCSR) will be sent to AMCs on monthly basis.

4. Organizing training workshop/s for ADR Monitoring Centres personnel to train on ADR reporting, data entry in Vigi-Flow, Causality assessment and on SOPs would be undertaken by NCC on a continuing basis.

5. Generation of reports at periodic intervals or as and when required by the Signal Review Panel and Steering Committee.
6. Review the list of drugs for focused ADR Monitoring suggested by the Strategic Advisory Committee or CDSCO and designates the focused drug monitoring to AMCs.
7. Signal detection and reporting to Signal Review Committee
8. Publication of safety newsletter on bi-annual basis.
9. Reporting to CDSCO about the functional status of AMCs.

2.3 Roles & Responsibilities of PvPI Personnel at Zonal CDSCO Offices

1. Zonal CDSCO Offices will provide administrative support to the ADR Monitoring Centres and report to CDSCO HQ
2. The disbursement of funds towards the conduct of workshop, office expenditures incurred by AMCs.

2.4 Roles & Responsibilities of PvPI Personnel at CDSCO Head Quarter

1. The yearly budget and expansion plan for PvPI will be formulated by the CDSCO
2. The decision of the steering committee on NCC reports will be forwarded to CDSCO.
3. The CDSCO will report to DTAB (Ministry of Health & Family Welfare)
4. The CDSCO is responsible for formulate and communicate safety related regulatory decisions for medicines.

3. List of CDSCO Zonal and Sub – Zonal Offices

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Proposed Sub Zonal Offices (2): Guwahati, Indore
4. The representation of Pharmacovigilance systems

Organogram of Pharmacovigilance Programme of India

Secretary-cum-Scientific Director of India Pharmacopoeia Commission

National Coordination Centre for PvPI

Steering Committee  Working Group  Secretary –cum-Scientific Director

Officer- in- charge
(Principal Scientific Officer)

Senior Scientific Officer

Scientific Assistants  Technical Associates

Finance and Administration
5. Programme Communications

Effective communication channels are the key to a successful running of PvPI. The following chart depicts the movement of information between the key stakeholders and ensures the continuous bidirectional nature of the transfer of data, information, and knowledge.

5.1 NCC Working Module

All the ADR reports from NCC are being continuously committed to the WHO - UMC.
5.1.1

Flow chart

Letter of Intent from AMCs Coordinator

Forwarded by HOD

NCC-PvPI

Examine the Suitability

Approved by AMC’s NCC

Vigi-Flow login details provided by NCC to AMCs

AMCs- To perform the Causality Assessment of the ADRs and furnish the mandatory fields in the Suspected ADRs form

AMCs - Upload the ADRs in Vigi-Flow

Send to

NCC-PvPI

Quality assessment by NCC-PvPI

Commit to

WHO - UMC (Sweden)

SAE, banned drugs, RTIs

CDSCO (HQ)

Signal

NCC-PvPI