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IPC

PHARMACOVIGILANCE PROGRAMME OF INDIA

GUIDANCE DOCUMENT FOR SPONTANEOUS ADVERSE DRUG REACTION REPORTING

Published by
Indian Pharmacopoeia Commission
(National Coordination Centre - Pharmacovigilance Programme of India)
Ministry of Health & Family Welfare
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2014

Guidance Document For Spontaneous Adverse Drug Reaction Reporting

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सत्यमेव जयते

भारत सरकार
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स्वास्थ्य एवं परिवार कल्याण मंत्रालय
Government of India
Department of Health and Family Welfare
Ministry of Health and Family Welfare

Message

The launch of the Pharmacovigilance Programme of India (PvPI) marks an important milestone in the country's march towards safe-guarding public health. PvPI is one of the indispensable steps taken by Ministry of Health and Family Welfare, Government of India for ensuring rational and safe use of medicines. No medicinal product is completely devoid of risk and a continuous monitoring of these products is required to ensure patient safety. Indian Pharmacopoeia Commission as National Coordination Centre (NCC) for PvPI with all their stakeholders is performing remarkably in achieving its mission and objectives. With their efforts India became the seventh largest contributor among the member countries participating in WHO Programme for International Drug Monitoring.

In order to maintain an efficient pharmacovigilance system in the nation awareness among medical professionals and public is required. NCC is working swiftly and effectively to promote understanding, education and training in pharmacovigilance. Adverse Drug Reaction reporting skills of healthcare professionals need to be improved to enhance the quality and quantity of reports.

This guidance document for reporting Individual Case Safety Reports will be helpful in developing and implementing a uniform reporting culture in the programme. Stakeholders are encouraged to follow these guidelines in specific contexts and to work jointly with NCC and Ministry of Health and Family Welfare in building upon and refining these to ensure a safe administration of medicine to the patients and creating a good healthcare system in the nation.

(Lov Verma)

New Delhi
12th May, 2014

Dr. G. N. Singh
Drug Controller General (India)
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Foreword

Three year ago, when Ministry of Health and Family Welfare, Government of India launched the Pharmacovigilance Programme of India and Indian Pharmacopoeia Commission as its National Coordination Centre (NCC), we made a commitment to ensure the safe and rational use of medicines being consumed in India. To renew and deepens this commitment various steps and strategies have been made by NCC including launch of PvPI helpline number to report ADRs, integration of Revised National Tuberculosis Control Programme with PvPI, PvPI tool kit, enrollment of new ADRs Monitoring Centres and a lot more are in pipeline. Over the past years PvPI has come up as the most credible program both in terms of planning and implementation.

Continuing Medical Education, training and workshops organized in different regions of the country to improve ADRs reporting practice and the attitude of healthcare professionals. NCC in collaboration with Central Drug Standard Control Organisation provides training and technical support to the stakeholders and this guidance document will be an important tool for conducting pharmacovigilance activities. The current version of guidance document will explore you with the various component of PvPI and helps in guiding the way to report ADRs.

(Dr. G. N. Singh)

Acknowledgement

We are pleased to present the first version of guidance document for Spontaneous Reporting of Adverse Drug Reaction. There has been tremendous growth in awareness and expansion in PvPI into identifying, analysing and minimizing the risk and promoting better and broader use of existing pharmacovigilance data for patient safety.

Valuable inputs that emerged during the guidance document review meeting and received from PvPI Working Group meeting in response to the manuscript preparation have given this a unique feature by incorporating value added information. The NCC is greatly indebted to the members of the Guidance Document Core Expert Committe to review the manuscript of the document. The inputs of all these experts are appreciated.

The inspiration and historical perspective were made available by Dr. G. N. Singh, Secretary-cum-Scientific Director, IPC, DCG(I), Dr. S. K. Gupta, Advisor, PvPI; Dr. Y.K. Gupta, National Scientific Coordinator, PvPI and Dr. Surinder Singh, Director, NIB for their strong recommendation to bring out this document for stakeholders on reporting adverse drug reactions. The NCC is especially indebted to Ministry of Health and Family Welfare for providing the infrastructural facilities required for carrying out this work uninterruptedly. Important suggestions were received from Dr. Bikash Medhi, Additional Professor & Joint Medical Superintendent, Department of Pharmacology, Coordinator PGIMER, Chandigarh; Dr. Suparna Chatterjee, Professor, Department of Pharmacology, Coordinator IPGMER, Kolkata; Dr. G. Parthasarathi, Professor & Head, Department of Clinical Pharmacy, Coordinator, JSS Medical College and Hospital, Mysore; Dr. Urmila Thatte, Professor & Head, Department of Clinical Pharmacology, Coordinator, Seth GS Medical College & KEM Hospital, Mumbai; Dr. Jitendra Kr. Sharma, Head, Division of Healthcare Technology, NHSRC, New Delhi and Dr. V. Kalaiselvan, Principal Scientific Officer, IPC. NCC is thankful for their valuable suggestions, support and encouragement in bringing out this publication. NCC also appreciates the inputs received from Dr. Vivek Ahuja, Director, Research & Development, PATH, Gurgaon, for his contribution as a Pharmacovigilance expert at the time of conceptualization of PvPI in 2010.

The NCC wishes to record its deep appreciation of the inputs by its staff particularly, Dr. Prasad Thota, Mr Vivek Dabas, Mr Ranvir Kumar, Mrs Surbhi Sharma, Ms Ismeet Kaur and Md. Iftekhar Hussain for updating the manuscript in the initial and final compilation of the guidance document.

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Table of Content

LIST OF ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
AEFI	Adverse Event Following Immunization
AIIMS	All India Institute of Medical Science
AMC	Adverse Drug Reaction Monitoring Centre
ATC	Anatomical Therapeutical Classification
CDSCO	Central Drugs Standard Control Organization
CIOMS	Council for International Organizations of Medical Sciences
DCG(I)	Drugs Controller General (India)
DIR	Detailed Investigation Report
ERI	Essential Requried Items
FIR	First Information Report
GVP	Good Pharmacovigilance Practice
HvPI	Haemovigilance Programme of India
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICSR	Individual Case Safety Report
IC	Information Component
IPC	Indian Pharmacopoeia Commission
MedDRA	Medical Dictionary for Regulatory Activities
NCC	National Coordination Centre
NHP	National Health Programme
NIB	National Institute of Biologicals
PIR	Preliminary Investigation Report
PV	Pharmacovigilance
PvPI	Pharmacovigilance Programme of India
SAE	Serious Adverse Event
TRRF	Transfusion Reaction Reporting Form
WHO-ART	World Health Organisation-Adverse Reactions Terminology
WHO-DD	World Health Organisation-Drug Dictionary
WHO-UMC	World Health Organisation-Uppsala Monitoring Centre

Introduction

Adverse reactions of drugs continue to remain as an important public health issue. Safety monitoring of medicines is the responsibility of all stakeholders of the healthcare system since it continues to be an important cause of morbidity and mortality. In some countries adverse drug reactions are among the leading causes of mortality. The safety of patients and the safe use of medicines are crucial for health policy development and delivery of the best healthcare. To prevent or reduce harm to patients thereby improving public health, the safety of medicines in clinical use must be monitored and evaluated through specialised systems. This requires a well-organised pharmacovigilance system to be established. Thus, a pharmacovigilance system is defined as a system used by an organisation to monitor the safety of authorised medicinal products and detect any change to their benefit-risk balance. A pharmacovigilance system is characterised by its structures, processes and outcomes. To run an effective pharmacovigilance system, a protocol is required for reporting adverse reactions associated with drug use. Therefore National Coordination Centre (NCC) aims to ensure the systematic and effective functioning of PvPI by publishing and implementing its guidance document for reporting Adverse Drug Reactions (ADRs).

This guidance document lays down requirements and guidance for reporting ADR and significant safety issues related to drugs regulated by the Central Drugs Standard Control Organization (CDSCO). This document does not establish legally enforceable responsibilities. This has been prepared by the NCC and approved by Working Group. The purpose of this document is to present the importance of pharmacovigilance in India, to record the growth and potential as a significant discipline within medical science, and to describe its impact on patient welfare and public health. This document also highlights the importance of collaboration and communication at local, regional and international levels to ensure that pharmacovigilance delivers its full benefits. It also provides guidance to stakeholders on good pharmacovigilance practices, assessment of data regarding drugs including vaccines and blood products.

Scope of Guidance Document

This document helps to expand the role and responsibilities of stakeholders under Pharmacovigilance Programme of India (PvPI) to identify, analyse and minimise the risk associated with drugs. Further it promotes better and broader use of pharmacovigilance data for patient safety by using the spontaneous reporting system.

The document is intended for the following stakeholders under PvPI:

- Professional staff at NCC and ADR Monitoring Centres (AMCs)
- Representatives of AMCs
- National Health Programmes integrated with PvPI
- Staff and consultants in CDSCO
- Healthcare practitioners (clinicians, dentists, pharmacists, nurses and other healthcare professionals)

Chapter 1: Pharmacovigilance Programme of India

1.1 Background

The Pharmacovigilance Programme of India was initiated by the Government of India in July 2010 with AIIMS, New Delhi as NCC for monitoring ADRs in the country for safe-guarding public health by assuring the safety of medicinal products. The NCC was shifted from AIIMS, New Delhi to IPC, Ghaziabad on 15th April 2011.

1.2 Overview

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 also detect adverse reactions but some of the important reactions, such as those, which take a long time to develop, or those, which occur rarely, may not be detected in the 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 medicinal products, a continuous post-marketing monitoring system is essential. PvPI provides such a system to collate the data and use the inferences to recommend regulatory interventions, besides communicating risks to healthcare professionals and the public.

The robust database will play a vital role in analysing and detecting new signals and updating the status of existing information on drug profile. The larger is the data for a 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. The Medical Colleges and hospitals are the corner stone of the PvPI. They act as AMCs which are responsible for collecting the Individual Case Safety Reports (ICSRs) and performing the follow up to obtain necessary supplementary detailed information for scientific evaluation of the cases. The ICSRs data is then entered into the databse by using VigiFlow software and constitutes the Indian patient safety database. VigiFlow also facilitates easy submission of Indian ICSRs to the WHO Global ICSRs Database, VigiBase.

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 drug safety and thereby reducing the risk associated with use of medicines.

1.5 Scope and Objectives

- To create a nation-wide system for patient safety reporting
- To identify and analyse new signal from the reported cases
- To analyse the benefit - risk ratio of marketed medications
- To generate evidence based information on safety of medicines
- To support regulatory agency 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 across globe
- To promote rational use of medicine

1.5.1 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

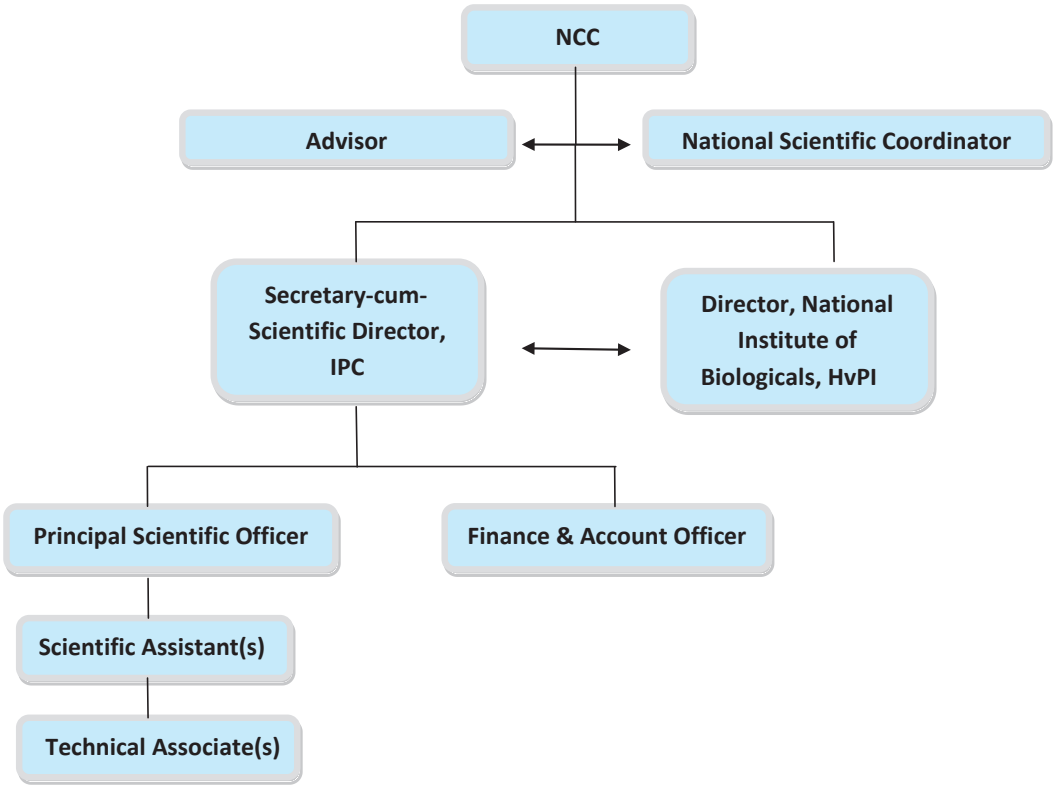
1.5.2 Long term goals

- To expand the pharmacovigilance programme to all hospitals (govt. & private) and centres 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

1.6 National Coordination Centre

Indian Pharmacopoeia Commission (IPC) is an autonomous institution of the Ministry of Health and Family Welfare, Government of India and functioning as National Coordination Centre for Pharmacovigilance Programme of India. The main responsibility of NCC is to monitor all the adverse reactions of medicines being observed in Indian population and to develop and maintain its own pharmacovigilance database for patient safety with respect to use of medicine in India so that regulatory interventions can be made based on Indian population. NCC is operating under the supervision of Steering Committee and Working Group which recommends procedures and guidelines for regulatory interventions. With a view to establish a centre of excellence for pharmacovigilance in India, NCC is participating in the WHO International Drug Monitoring Programme and collaborating with the WHO-Uppsala Monitoring Centre, Sweden. IPC also sets standards for drugs that are manufactured, sold and consumed in India. It further publishes Indian Pharmacopoeia and National Formulary of India to improve quality of medicine and promotes rational use of generic medicine.

1.6.1 Organogram of NCC



1.6.2 Committees under NCC

The following committees and panels are constituted by Ministry of Health and Family Welfare, Government of India to give proper direction for efficient functioning of the programme.

Steering Committee

PvPI is administered and monitored by Steering Committee to supervise and give proper direction to the programme.

Working Group

It is constituted to approve major technical issues related to establishment and implementation of programme and giving technical inputs to CDSCO for regulatory intervention of medicine.

Quality Review Panel

It is constituted to review quality, causality assessment and completeness of ICSRs. The panel also makes recommendations to PvPI working group after data analysis and will devise formats and guidance documents for follow up actions after implementation of recommendations.

Signal Review Panel

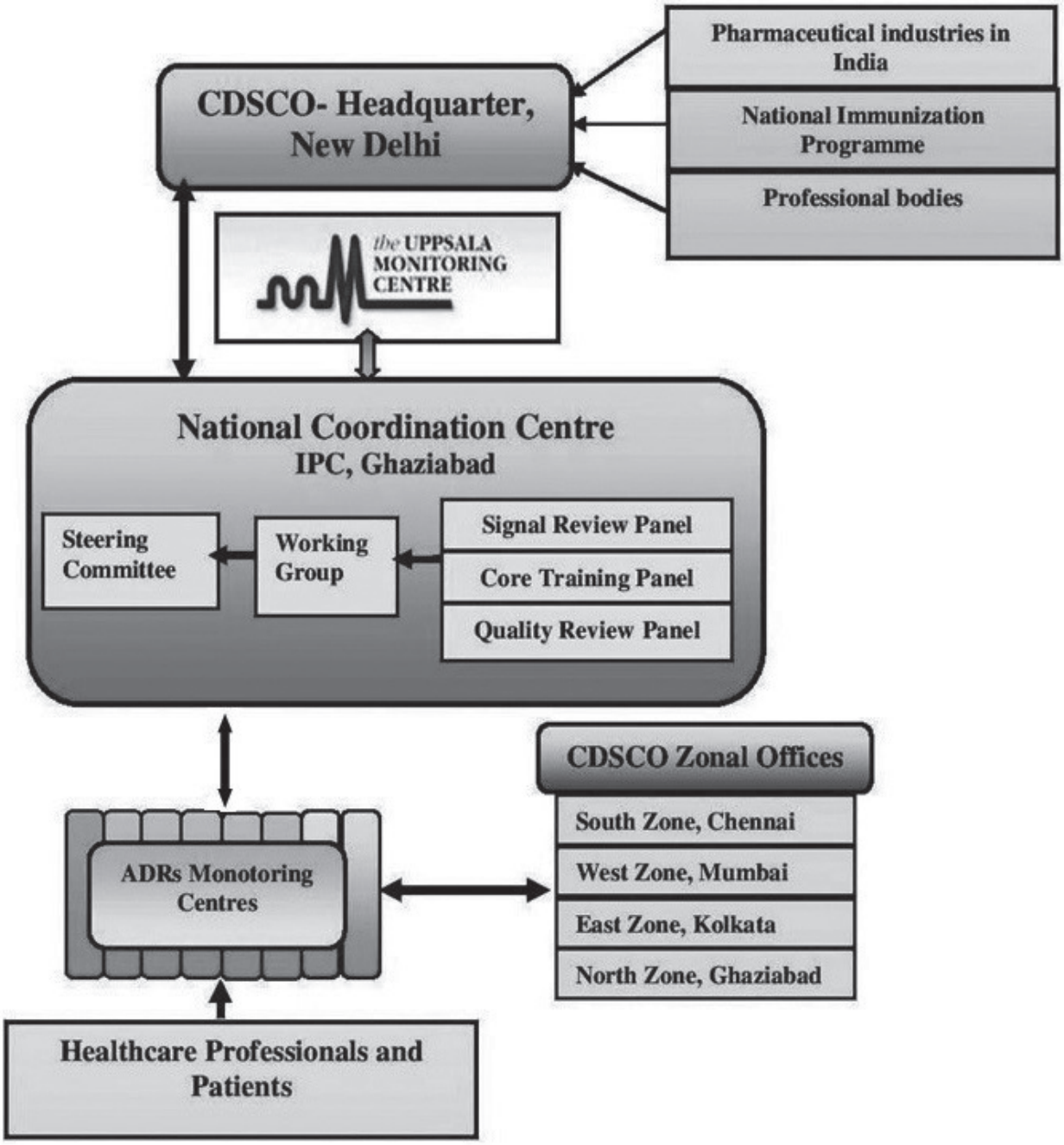
It is constituted of experienced scientists and clinical experts affiliated to government and non-government academic institutions and hospitals to indentify and evalute the signals from ICSRs submitted to NCC. This panel assesses the results of the regular computerized screening of ICSRs in NCC database for the occurrence of signals of possible importance of public health, drug regulation and science. It also defines biostatistical methods to be followed for analysis and creates standardized post analytical reports that will help in understanding the information that is derived from ADRs. It is also responsible to decide on actionable indicators.

Core Training Panel

The Core Training Panel of PvPI identifies trainers and zone wise training centers for imparting training under pharmacovigilance training programme. Core training panel interacts with international agencies for participation and implementation of training programs related to pharmacovigilance. It organizes training and projects budgetary requirements. Training modules and training schedules are also developed by this panel.

1.7 Communication under PvPI

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



PvPI - Communication

Chapter 2: Responsibilities of PvPI Stakeholders

2.1 Responsibilities of Stakeholders

2.1.1 Personnel at AMC

Each AMC under PvPI is assigned with a coordinator and a technical associate responsible for its functioning. Their roles and responsibilities are:

- The designated coordinator is responsible for the proper functioning of respective AMC. In absence of the coordinator, the designated deputy coordinator is responsible for the smooth functioning of the centre.
- Other important responsibilities of coordinator include ensuring quality, integrity and completeness of a valid case, causality assessment and scrutinizing the ADR reports as per SOPs.
- The technical associate is responsible for collecting ICSRs and ensuring proper follow up. All the scrutinized and signed ADR reports should be entered in VigiFlow by the technical associate. Every report has to be sent for the central assessment at NCC.
- The centre coordinator is responsible for sending the monthly reports of their AMC to NCC.
- The centre coordinator is also responsible for sensitization of the Health Practitioners (clinicians, dentists, pharmacists, nurses and other healthcare professionals) of the catchment hospital for spontaneous ADR reporting by various modes (e.g. lectures on ADR reporting, pamphlets & newsletters).
- Feedbacks to the ADRs reporter.

2.1.2 Personnel at NCC

NCC is responsible for:

- Preparing Standard Operating Procedures (SOPs), guidance documents and training manuals.

- Enrolment of new AMC.
- Reviewing and analyzing ICSRs received from AMCs and forwarding them to WHO-UMC.
- Organising Continuous Medical Education (CME) on pharmacovigilance at various AMCs.
- Conducting periodic training and workshops for all enrolled AMCs.
- Publishing the PvPI Newsletter on timely basis.
- Reporting all concerned issues to CDSCO HQ.
- Providing procurement, financial and administrative support to all AMCs enrolled under PvPI.
- Communicate with WHO-UMC for administrative logistic and technical issues with respect to PV activities.
- Represent PvPI in international meetings e.g. annual meetings organized by WHO.
- Token of appreciation for the ADR reporters.

2.1.3 Personnel at Zonal/Sub-zonal CDSCO office

The Zonal/Sub-zonal is responsible for:

- Reporting all drug safety issues to the CDSCO headquarter and NCC-PvPI.
- Providing administrative and logistic supports to the AMC at their zone.
- Auditing/inspecting AMC in their respective zonal and submitting the inspection report to CDSCO HQ.

2.1.4 Personnel at CDSCO HQ

The CDSCO HQ is responsible for:

- Taking appropriate regulatory decision and actions regarding drug safety.
- Propagating medicine safety related decisions to stakeholders.
- Providing administrative and Technical support to run PvPI.

2.1.5 Personnel at National Health Programs

The National Health Programs integrated with PvPI can coordinate with NCC or nearest AMC to report ADR occurred with the medicines used in their respective programme.

2.2 Training to Stakeholders

There are four below mentioned regional centres under PvPI recognized as 'Regional Resource Centre'.

- EASTERN REGION: Department of Pharmacology, Institute of Post Graduate Medical Education & Research (IPGMER), Kolkata
- WESTERN REGION: Department of Clinical Pharmacology, Seth GS Medical College and King Edward Memorial (KEM) Hospital, Mumbai
- NORTHERN REGION: Department of Pharmacology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh
- SOUTHERN REGION: Department of Clinical Pharmacy, Jagadguru Sri Shivarathreeswara (JSS) Medical College Hospital, Mysore

These Regional Resource Centres provide training and technical supports to the newly enrolled AMCs and all other stakeholders under PvPI in their respective regions and support the expansion of PvPI. The training programmes conducted by these Regional Resource Centres should required prior intimation and approval from the NCC. The training would be conducted in a standardized manner as per the format suggested in the training module.

2.2.1 Roles and Responsibilities of Regional Resource Centres

- To provide basic concepts, terminologies and SOPs to the newly enrolled AMCs by training and workshop
- To provide hands-on training on ADR form filling, VigiFlow data entry and various other aspect of PvPI.
- To provide resource materials to the new centres
- Interaction on regular basis to resolve the technical issues with the AMCs

Chapter 3: Reporting of Adverse Drug Reactions

Adverse drug reactions can be monitored through two ways:

1. Active surveillance system
2. Passive surveillance system

Passive surveillance means no active measures are taken to look for adverse effects other than the encouragement of healthcare professionals and others to report safety concerns. Reporting is entirely dependent on the initiative and motivation of the potential reporters. Spontaneous or voluntary reporting is a type of passive surveillance. Active surveillance, in contrast to passive surveillance requires a continuous pre-organised process. An example of active surveillance is the follow-up of patients treated with a particular medicinal products as in the Cohort Event Monitoring (CEM).

3.1 Spontaneous Reporting

A spontaneous report is an unsolicited communication by healthcare professionals or consumers, pharmaceutical company to NCC or other organization (CDSCO, AMCs) that describes one or more suspected ADR in a patient given a medicinal product that does not drive from study or any organised data collection scheme. Presently PvPI is following spontaneous reporting system to collect data on drug safety.

3.2 Suspected Adverse Drug Reaction Reporting Form

The NCC has designed a 'Suspected Adverse Drug Reaction Reporting Form' to record adverse reactions related to drugs (page no 14). Separate forms are available to record adverse reactions associated with transfusion of blood and blood related products and Adverse Event Following Immunization (AEFI). A report that contains information describing a suspected ADRs related to the administration of one or more medicinal products to an individual patient is termed as ICSR. Following are the points to be filled in an ADR form.

A. Patient Information

1. *Patient initials:* Write only the initials of a patient instead of full name. For e.g.: Madhu Gupta should be written as MG.

2. *Age at time of event or date of birth:* Write either the date of birth or age of the patient at the time of event or reaction occurred.

3. *Sex:* Mention the gender of the patient.

4. *Weight:* Mention the weight of the patient.

B. Suspected Adverse Reaction

5. *Date of reaction started:* Mention the date on which the reaction was first observed.

6. *Date of recovery:* If the reaction recovered, the date on which the patient recovered from the reaction should be report.

7. *Describe reaction:* Provide the description of the reaction in terms of nature, localization etc. For example patient developed erythematous maculopapular rash over upper and lower limb.

C. Suspected Medications

8. The details of suspected medication(s) such as *drug name (brand or generic name), manufacturer, batch no/lot no, expiry date, dose used, route used, frequency, dates of therapy started and stopped, and indication* should be provided by the reporter.

9. *Dechallenge details:* Mention the status on dechallenge as:
   - **'Yes'**- if reaction abate after dechallenge
   - **'No'**- if reaction did not abate after dechallenge
   - **'Unknown'**- if effect of dechallenge is not known
   - **'Not Applicable' or 'NA'**- if dechallenge is not applicable as in case of vaccines, anaesthesia, where single dose is given, death, or treatment is completed prior to reaction or event
   - **'Reduced dose'**- If dose at which the reaction occurred is reduced

   Note: Also mention the reduced dose and date.

10. *Rechallenge details:* Mention the status on rechallenge as:
    - '**Yes'**- if reaction reappeared after rechallenge
    - **'No'**- if reaction does not reappear after rechallenge
    - **'Unknown'**- if effect of rechallenge is not confirmed
    - **'Not Applicable' or 'NA'**- if rechallenge is not applicable as in case of anaphylaxis reaction
    - **'Re-introduced dose'**- Mention the dose and date of rechallenge

11. *Concomitant drugs:* Write the details of all concomitant drugs including self-medication, OTC medication, herbal remedies with therapy dates.

12. *Relevant tests/ laboratory data:* Mention all laboratory data (if available) relevant to the reaction occurred.

13. *Other relevant history:* Write the relevant history persistent to patient including pre-existing medical conditions (e.g. allergies, pregnancy, smoking, alcohol use, hepatic/ renal dysfunction) and concurrent condition can be describe in this section.

14. *Seriousness of the reaction:* If any reaction is serious in nature, tick the appropriate reason for seriousness as:

- **'Death'**- if the patient died due to adverse event

Note: Mention the death cause & date in the seriousness of the reaction.

- **'Life-threatening'**- if patient was at substantial risk of dying at the time of the adverse event
- **'Hospitalisation/prolonged'**- if the adverse event caused hospitalisation or increased the hospital stay of the patient
- **'Disability'**- if adverse event resulted in a substantial disruption of a person's ability to conduct normal life functions
- **'Congenital anomaly'**- if exposure of drug prior to conception or during pregnancy may have resulted in an adverse outcome in the child.
- **'Required intervention to prevent permanent impairment/damage'**- if medical or surgical intervention was necessary to preclude permanent impairment of a body function, or prevent permanent damage to a body structure
- **'Other' -**when the event does not fit above conditions, but the event may put the patient at risk and may require medical or surgical intervention to prevent one of the above conditions. Examples include serious blood dyscrasias (blood disorders) or seizures/convulsions that do not result in hospitalization, development of drug dependence or drug abuse

15. *Outcomes:* Tick the outcome of the event as:

- **'Fatal'**- if the patient dies
- **'Continuing'**- if the patient is continuing to experience the reaction
- **'Recovering'**- if the patient is recovering from the reaction

- **'Recovered'**- if the patient has completely recovered from the reaction (mention the date of recovery)
- **'Unknown'**- if the outcome is not known

D. Reporter

16. *Name and Professional address:* A reporter must mention his/her name and professional address on the form. The identity of the reporter will be maintained confidential

17. *Causality assessment:* The reporter (if trained) must perform the causality assessment and justify the assessment

18. *Date of report:* Mention the date on which he/she reported the adverse event.

Collect all the information required to be filled in the suspected ADR reporting form. In case complete information is not available fill all the Essentially Required Items (ERI) for a quality ICSR. In case ERI are not available make sure that the form contains all the mandatory fields.

Mandatory Fields	Essentially Required items
Patient initials, age at onset of reaction, reaction term(s), date of onset of reaction, suspected medication(s) and reporter's information.	Patient initials, age at onset of reaction, gender, reaction term(s), date of onset of reaction, suspected medication(s), dose, date of therapy started, indication of use, seriousness, outcome, dechallenge and rechallenge details, reporter's information and date of report.

Note: For a valid case report mandatory fields are the minimum requirement.

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by healthcare professionals

INDIAN PHARMACOPOEIA COMMISSION
(National Coordination Centre-Pharmacovigilance Programme of India)
Ministry of Health & Family Welfare
Government of India
Sector-23, Raj Nagar, Ghaziabad-201002
www.ipc.nic.in

(AMC/ NCC Use only)
AMC Report No.
Worldwide Unique

A. PATIENT INFORMATION

1. Patient Initials _____

2. Age at time of Event or date of birth _____

3. Sex ☐ M ☐ F

4. Weight ____Kgs

12. Relevant tests / laboratory data with dates

B. SUSPECTED ADVERSE REACTION

5. Date of reaction started (dd/mm/yyyy)

6. Date of recovery (dd/mm/yyyy)

7. Describe reaction or problem

13. Other relevant history including pre-existing medical conditions (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/ renal dysfunction etc)

14. Seriousness of the reaction

- ☐ Death (dd/mm/yyyy)
- ☐ Life threatening
- ☐ Hospitalization/prolonged
- ☐ Disability
- ☐ Congenital-anomaly
- ☐ Required intervention to prevent permanent impairment / damage
- ☐ Other (specify)

15. Outcomes

- ☐ Fatal
- ☐ Continuing
- ☐ Recovering
- ☐ Recovered
- ☐ Unknown
- ☐ Other (specify)

C. SUSPECTED MEDICATION(S)

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
								Date started	Date stopped	
i.										
ii.										
iii.										
iv.										

S.No As per C	**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)

D. REPORTER (see confidentiality section on first page)

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)

SPECIMEN COPY

3.3 Who can Report?

All healthcare professionals (clinicians, dentists, pharmacists, nurses etc) and non-healthcare professionals including consumers can report suspected adverse drug reaction. Pharmaceutical companies can also send ICSRs specific for their product to NCC.

3.4 Why to Report?

As a healthcare professional, it is a moral responsibility to report adverse reactions associated with use of medicines and safeguard the health of public. The safety of more than 1.2 billion population is a concern and occurrence of ADR constitutes a significant economic burden on the patient and government. India has a vast genetic and ethnic variability with different disease prevalence. Use of multi-modal practices, poor patient compliance are the other factors requires ADR reporting.

3.5 What to Report?

In order to foster the culture of reporting, PvPI encourages reporting of all types of suspected ADRs- irrespective of whether they are known or unknown, serious or non-serious, frequent or rare and regardless of a established causal relationship. Although pharmacovigilance is primarily concerned with pharmaceutical medicines and vaccines, adverse reactions associated with drugs used in traditional medicine (e.g. herbal remedies), medical devices, contrast media and other pharmaceuticals will also be consider. Special fields of interest are outcomes associated with the drug use in pregnancy, lactation, paediatric and geriatric. In addition, the reporting of ADRs due to lack of efficacy, overdose, antibiotic resistance and suspected pharmaceutical defects (spurious and adulterated drugs) is recommended. Reporting of ADRs encountered with abuse, off-label use, misuse or occupational exposure is not currently included in PvPI, however physician judgement shall be final.

3.6 How and Whom to Report?

Use the 'Suspected Adverse Drug Reaction Reporting Form' which is available on the official website of IPC (www.ipc.gov.in) as well as CDSCO (www.cdsco.nic.in) to report any ADR. Reporters from AMCs after filling the above mentioned Suspected ADR Reporting form can submit it to the coordinator or technical associate of the respective AMC. A reporter who is not a part of AMC can submit the filled ADR form to the nearest AMC or directly to the NCC. A reporter can also mail the form at pvpi.ipcindia@gmail.com.

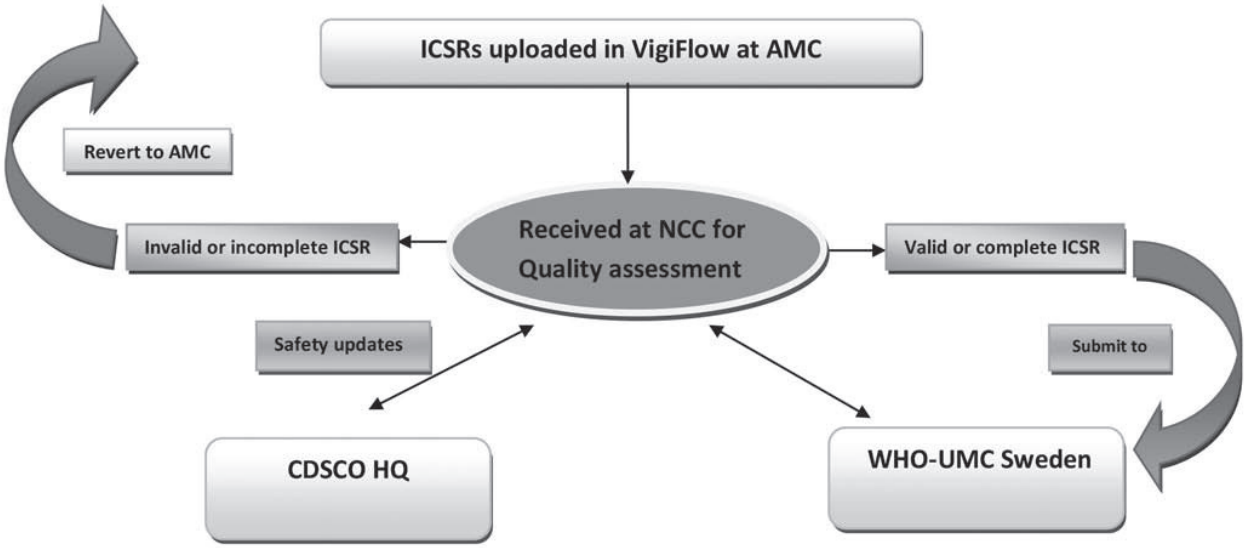
NCC-PvPI also created a helpline number **1800-180-3024** to report adverse reactions associated with medicinal products. A reporter can also call on this number to report ADRs from 9:00 am to 5:30 pm in weekdays.

3.7 Establishment of an AMC

A 'Letter of Intent' is required to be submitted by the Heads of the Institutions to participate in this nationwide programme to monitor drug safety. After examining the suitability, the concerned centre may be inducted as AMC under PvPI. Subsequently, NCC communicates the AMC details to WHO- UMC to obtain VigiFlow (WHO-UMC global software) login details to upload ICSRs.

3.8 Data Flow

Once the medical institute is enrolled as an AMC, the AMC starts reporting ADRs to NCC. Following chart explains the flow of data at regional, national and international level.



3.9 Assessment of Individual Case Safety Reports

The quality of the ICSR will be assessed for completeness of information and it will be reviewed for:

1. ***Quality of documentation:*** e.g. completeness and integrity of data, quality of diagnosis, follow-up.
2. ***Coding:*** Drug name and reaction term (use WHO Drug Dictionary to code a drug and WHO Adverse Reaction Terminology to code an adverse reaction term)
3. ***Relevance:*** with regard to the detection of new reactions, drug regulation, scientific or educational value. The following questions especially may be asked:
    - ***New drug -*** a new drug shall continue to be considered as new drug for a period of four years from the date of its first approval or its inclusion in IP, whichever is earlier.
    - ***Unknown reaction-*** Not included in pack insert of the product
    - ***Serious reaction-*** Refer to point number (3.1.C.14)
4. ***Identification of duplicate*** **reports:** Certain characteristics of a case (sex, age or date of birth, date of drug exposure, etc.) may be used to identify duplicate reporting.
5. ***Causality assessment*****:** Case reports describe suspected ADRs. The likelihood of a causal relationship between drug exposure and adverse events must be validated. (refer to Chapter 6)

3.10 Utilization of the Data

Data collected in pharmacovigilance can be used in a variety of ways:

1. ***Signal generation and*** **strengthening:** A major aim of pharmacovigilance is the early detection of signals with regard to possible adverse reactions. A signal may be strengthened by further analysis can help the regulatory system in performing regulatory activities. (refer to Chapter 7)
2. ***Risk Management:*** The identification, assessment, and prioritization of risks followed by coordinated and economical application of resources to minimize, monitor, and control the probability and impact of unfortunate events is known to risk management. (refer to Chapter 9)
3. ***Drug regulation*****:** After approval of a medicinal product, all available domestic and international safety information is continuously monitored by the CDSCO and market authorisation holders. The PvPI data can be useful in review of product safety information and implementation of required changes in the prescribing information/pack insert.
4. ***Education*****:** The information from PvPI data is useful in updating the knowledge associated with the use of medication to health care professionals.

3.11 Reporting Requirements in Special Population

3.11.1 Pregnancy and Breastfeeding

Pregnancy

The clinical trial program of a medicinal product under development rarely includes pregnant women, unless the product is intended specifically for use during pregnancy. All pregnant women coming for routine pre-natal check-ups must be monitored by the healthcare professionals for medication use. Patients must be followed-up to collect information on the outcome of the pregnancy and development of the child after birth. At present NCC database contains a limited number of ICSRs related to parent-child case. Intensive monitoring is required to draw any conclusion to upgrade/downgrade pregnancy category of drugs use during pregnancy.

Breastfeeding

All lactating mother exposed to medicinal product should be monitored to collect information on outcome of lactation on neonates and infants.

3.11.2 Paediatric and Geriatrics

The collection of safety information in the paediatric and geriatric population is important as ADRs can lead to significant morbidity and death among these populations. Immunisation is one of the most common and widely used public health interventions in paediatric population. On other hand geriatric population is at higher risk of developing ADRs due to factors like polypharmacy and co-morbidities. The paediatric and geriatric population are more vulnerable to some adverse reactions. Therefore, data collected from this program will provide a national database for drug safety information in these vulnerable populations. To ensure safe and effective medicines for children and elderly, efforts are needed at different levels (CDSCO, pharmaceutical industries, health care professionals, and parents). NCC database contains ICSRs reported for paediatric population and geriatric population but more number of case reports are required for monitoring drug safety in these populations. Population Specific treatment guidelines can be drawn using NCC database for these populations.

3.11.3 Reporting in the Event of a Public Health Emergency

A public health emergency is a public health threat duly recognised either by the WHO or Ministry of Health and Family Welfare, Government of India. In the event of a public health emergency, regular reporting requirements may be amended.

Chapter 4: Haemovigilance Programme of India (HvPI)

4.1 Introduction

Haemovigilance Programme of India (HvPI) is a process of data collection and analysis of transfusion -related adverse reactions in order to investigate their causes and outcomes and prevent their occurrence or recurrence. IPC in collaboration with National Institute of Biologicals (NIB) has launched Haemovigilance across the country under PvPI with following terms of references:

1. To track Adverse Reactions/ Events and incidence associated with Blood transfusion and Blood product administration (Haemovigilance).

2. To help in identifying trends, recommend best practices and interventions required to improve patient care and safety, while reducing overall cost of the healthcare system.

HvPI was launched on 10th Dec 2012 as an integral part of PvPI. NIB is functioning as NCC to collate & analyze adverse reaction data for blood and blood products.

Further information on Haemovigilance is available on http://nib.gov.in/haemovigilance1.html

4.2 Transfusion Reaction Reporting Form (TRRF)

Transfusion Reaction Reporting Form (TRRF) for Blood & Blood Products

Indian Pharmacopoeia Commission – National Institute of Biologicals
Ministry of Health & Family Welfare – Govt. of India
HAEMOVIGILANCE
(Pharmacovigilance Programme of India)

TRANSFUSION REACTIONS REPORTING FORM FOR BLOOD & BLOOD PRODUCTS

For reporting of Transfusion Reactions by Healthcare Professionals

A) PATIENT INFORMATION * Mandatory Field

Patient initials* ..... DOB/Age in years *: ..... Blood Group *: _____ Diagnosis .....Hospital Code No*.....

Hospital Admission No. * _____ Sex: * F ☐ M ☐

Date & Time of Transfusion * ..... Date & Time of reaction* ..... Date & Time of recovery.....

B) TRANSFUSION PRODUCT DETAILS*

Components	Select Components	Unit Number (transfused)	Expiry Date	Manufacturer	Batch Number	Indications	1st time / Repeat Transfusion (No. of Repeats)
Whole Blood							
Red Blood Cells							
Platelets Apheresis							
Platelets Pooled/ RDP							
Solvent detergent (SD) Plasma							
FFP							
Cryoprecipitate							
Any other							

Blood Products (Please Specify)	Manufacturer	Batch Number	Expiry Date		

C) NATURE OF ADVERSE REACTIONS *

	Reactions	Please Tick (√)
1	Immunological Haemolysis due to ABO Incompatibility	
2	Immunological Haemolysis due to other allo- antibodies	
3	Non Immunological Haemolysis	
4	Transfusion Transmitted Bacterial Infection	
5	Anaphylaxis / Hypersensitivity	
6	Transfusion Related Acute Lung Injury (**TRALI**)	
7	Transfusion Transmitted Viral Infection (**HBV**)	
8	Transfusion Transmitted Viral Infection (**HCV**)	
9	Transfusion Transmitted Viral Infection (**HIV-1/2**)	
10	Transfusion Transmitted Viral Infection, other (**Specify**)	
11	Transfusion Transmitted Parasitic Infection (**Malaria**)	
12	Transfusion Transmitted Parasitic Infection, other (**Specify**)	
13	Post Transfusion Purpura	
14	Transfusion Associated Graft versus Host Disease (**TAGvHD**)	
15	Febrile Non Haemolytic Reactions(FNHTR)	
16	Transfusion Associated Dyspnea(TAD)	
17	Transfusion Associated Circulatory Overload (TACO)	
18	Other Reaction(s)	

D) OUTCOMES OF THE ADVERSE REACTIONS*

- Death following the adverse reactions ☐
- Recovered ☐
- Recovered with sequelae ☐
- Permanently disabled ☐
- Unknown ☐

Any other information .....

E) REPORTER *

Name and professional Address: _____

_____

Pin Code : _____ Email: _____

Tel No. (with STD code)_____

F) CAUSALITY ASSESSMENT*

Date of this report (DD/MM/YYYY)

Chapter 5: Guidance for Reporting Adverse Event following Immunization

5.1 Introduction

AEFI is defined as a medical event that takes place after immunization, causes concern and is believed to be caused by immunization. The AEFI should be handled effectively in order to maintain/restore public faith in immunization program. AEFI Surveillance System in India has come a long way since its inception in 1986.

To ensure their safety and efficacy, vaccines are subjected to release a lot at Central Research Institute, Kasauli before release for public use. AEFIs may occur due to the intrinsic property of vaccines and constituents like stabilizers, adjuvant, antibiotics, diluents etc. added to the vaccines or hypersensitivity of some individuals to vaccine component(s). Such incidents are rare but may become apparent in terms of number when vaccinating a large cohort. AEFI may also result from programme errors as a result of inappropriate storage, improper handling, preparation and administration etc. of vaccines. AEFI surveillance and timely management will build public confidence and prevent additional clustering of cases if they occur due to a programme error.

AEFI surveillance monitors immunization safety, detects and responds to adverse events; corrects unsafe immunization practices, reduces the negative impact of the event on health and contributes to the quality of immunization activities. In India, the safety of vaccines is monitored by the division of AEFI, Ministry of Health and Family Welfare, Government of India and PvPI. Intensive efforts are being made to strengthen surveillance and monitoring of AEFI in the country.

A reporter can report AEFI cases either to AMC or NCC. AEFI cases reported to PvPI are further coordinated with national level AEFI committee and State Expanded Programme Immunization Officers for reporting and investigation. Subsequently, AEFI committee follows with local AEFI team to completely furnish FIR/PIR/DIR to do the causality assessment.

5.2 Adverse Events following Immunization - Reporting Form

5.2.1 FIRST INFORMATION REPORT FORM

First Information Report

Adverse Events Following Immunization

(To be reported within 48 hrs to the GoI)

State	District
Block	Date of report
Name	
Age (DOB)	Sex: Male/ Female
Mother's / Father's Name	
Complete Address of the case	
Date & time of vaccination	Date & time of onset of symptoms
Complete address of place of vaccination	
Vaccines given	
Batch Number & Expiry date of each vaccine	
Type of reaction	
Date of Death	
Any other comment[1]	

Name of person filling the report

Signature and Designation

5.2.2 PRELIMINARY INVESTIGATION REPORT FORM

PRELIMINARY INVESTIGATION REPORT
Adverse Events Following Immunization

(To be reported within 7 DAYS to the GoI)

State	District
Block	Date of report
Name:	
Age (DOB):	Sex: Male/ Female
Mother's / Father's Name	
Complete Address of the case	
Date & time of vaccination	Date & time of onset of symptoms
Vaccines given	
Complete address of place of vaccination	
Batch Number & Expiry date of each vaccine	
Type of reaction	
Date of Death	
Probable cause of death:	
Probable cause of the AE: Programme error/ Vaccine reaction/ Coincidental/ Unknown	
Further action planned: Yes/ No (if Yes Details)	
Any other comment	

Name of person filling the report

Signature and Designation

5.2.3 DETAILED INVESTIGATION REPORT FORM

DETAILED INVESTIGATION REPORT

Adverse Events Following Immunization (AEFI)

(To be reported within three months)

Adverse event following Immunization or Death after Immunization

Date of Investigation: Case ID No.: IND (AEFI)/_ _ /_ _ _ /_ _ / _ _ _ Use same coding as done for AFP cases

1	Name of child affected (In Block Letters)	
2	Name of Parents	Father's name Mother's name
3	Age and Sex	— —/— —/— — Date of Birth Male/ Female yrsmo days (if know)
4	Full detailed address	
5	Place of immunization	Health facility/ Out reach session site/Field camp/ Hospital/ Maternity home/ Private clinic/ any other place
6	a. Date and time of immunization	
	b. Location of immunization session (Full address)	
7	No. of children immunized at the session	BCG___ DPT1___ DPT2___ DPT3___ DPT B___ OPV1___ OPV2___ OPV3___ OPV B___ HEPB 1___ HEPB 2___ HEPB 3___ MEASLES___ DT___ TT1___ TT2___ TT B___ VIT A___ OTHERS___
8	Date and time of onset of	
9	AEFI Date of Initial report	

9	Type of AEFI	
10	Was the patient admitted to hospital	Yes/ No/ Unknown
11	If Yes, date & Time of admission	
	Name of Hospital	
	Ward no	
	Centralized admission number	
	Outcome	Recovered/ still in hospital/ death/ unknown/ Residual problem
12	SYMPTOMS AND SIGNS	
	a. Time of onset	
	b. Sign of shock present/absent	
	c. Temperature	
	d. Pulse	
	e. Respiration	
	f. Convulsion	
	g. Vomiting	
	h. Diarrhoea	
	i. Altered sensorium	
	j. Rash	
	k. Any other symptoms & sign (pl specify)	
	l. Progress of symptoms and signs with brief history & chain of events (Please attach additional sheet if required or patient records if available)	

	m. Mention whether above sign and symptoms are seen by investigating officer or whether above sign and symptoms are noted from hospital record	
13	Treatment given (attach copy of case sheet, if available)	
14	GROWTH & DEVELOPMENT/PAST/ FAMILY HISTORY (please fill as relevant to case)	
	a. Type of Delivery	Normal delivery/ LSCS/ Assisted birth
	b. Gestation	Full term/Premature/Post dated
	c. Complications during birth	
	d. Birth weight (if possible)	
	e. Present Weight (if possible)	
	f. Present length/ height (if possible)	
	g. Present head circumference (if possible)	
	h. Developmental milestones	Gross motor
		Fine Motor
		Language
		Adaptive & Social
	i. Past illness like allergy, asthma, convulsion etc	
	j. Any previous history of similar event after immunization	Yes/ No/ Unknown
	k. Family history - history of epilepsy, allergy, asthma etc in the family	

	l. Any history of similar event in siblings	Yes/ No/ Unknown
	m. Was the child on any concurrent medication for any illness	Yes/ No/ Unknown If yes: Indication & Dosage
15	INFORMATION ON IMMUNIZATION (IN CASE PROGRAMME ERROR SUSPECTED)	
	a. Name of worker who administered vaccine	
	b. Designation	
	c. Length of service	
	d. Experience	
	e. When did worker receive the last training in immunization	
	f. Name of Health Assistant (Supervisor)	
	g. Designation	
	h. Length of service	
	i. Experience	
	j. When did Health Assistant (Supervisor) receive the last training in immunization	
16	k. Total number of mother and children immunized. Attached detailed list giving name/age/sex/vaccines given	
	l. Any history of similar event reported (among those vaccinated)	a. At same clinic: Yes/ No/ Unknown b. Using same vaccine type at previous clinic sessions: Yes/ No/ Unknown
	If Yes	Specify event Number Place

	m. Any history of similar event reported (among unimmunized)	a. At same clinic session: Yes/ No/ Unknown b. In the field: Yes/ No/ Unknown
	If Yes	Specify event Number Place
	n. At what stage was the index child immunized	a. Within the first few doses of the vial b. Within the last few doses of the vial c. Within the first vaccinations of the clinic session d. Within the last vaccinations of the clinic session e. Unknown
	o. Vaccination technique (observe the relevant vaccinator)	Reconstitution: Satisfactory/ Unsatisfactory/ Not observed
		Drawing of vaccine: Satisfactory/ Unsatisfactory/ Not observed
		Injection technique: Satisfactory/ Unsatisfactory/ Not observed
17	DETAILS OF VACCINE GIVEN PRIOR TO AEFI	
	a. Date of receipt of vaccine of implicated batch by	MoH/ State Regional Store District PHC/CHC/ Urban Health Center Sub center/ Out reach session site
	b. Status of maintenance of cold chain at	State
		Regional store
		District Head Quarter
		PHC/ Urban health post
		Subcenter
		Session Site
	c. Is there a suspicion of breach of cold chain as per records? (If so, when & where?)	

	m. Time of receipt of vaccine at field camp site (immunization session site)	
	n. Maintenance of cold chain during transit from Health Post/ PHC to field camp site	
	o. Name of person collecting vaccine from fixed centre to field camp site	
	p. Vaccines used	BCG/ DPT/ OPV/ Measles/ Hepatitis/ Vit A/ others (specify)
	q. If reconstituted, what diluent was used	
	r. Which type of syringe was used for reconstitution?	Reusable/ Disposable/ AD
	s. Practice of reconstitution	Same syringe used for multiple vials of same vaccine/ Same syringe used for reconstituting different vaccines/ Separate syringe for each vial/ Separate syringe for each vaccine
	t. Is the needle left in reconstituted vaccine vial	Yes/ No/ Not observed
	u. Whether label of vial intact i) Batch No ii) Expiry date iii) Manufactured by	
	v. Date and time when vial opened	
	w. Date of vaccine sent for testing	
	x. Result of sample of vaccine sent for testing	
	y. Is the vaccine collected by FDA or SRA	
	i) Name of the officer	
	ii) Date when vaccine sent for testing	

	iii) Place where vaccine sent for testing	
	iv) Result of vaccine sent for testing	
18	STERLISATION OF SYRINGE AND NEEDLE	
	a. Types of syringes used to vaccinate the child.	Reusable/ Disposable/ AD
	b. Method of sterilization if reusable syringes used	
	c. Name and Designation of person who was responsible for autoclaving/ boiling for 20 minutes	
	d. Date and time of autoclaving/ boiling started	
	e. Date and time of autoclaving/ boiling completed	
	f. Sterilization satisfaction as per records of Signolac strip register	
	g. No of syringes & needles autoclaved	
	h. No of syringes & needles used for the session.	
19	INVESTIGATIONS DONE	
	a. Whether any blood tests were done	
	b. If yes, results of blood tests	
	c. Whether CSF was examined	
	d. If yes, result of CSF tests	

Chapter 6: Causality Assessment of Adverse Event

6.1 Definition

Causality Assessment is defined as the evaluation of the likelihood that a medicine was the causative agent of an observed adverse event.

6.2 Why Causality Assessment?

An inherent problem in pharmacovigilance is that most case reports concern *suspected* ADR. Adverse reactions are rarely specific for the drug, specific diagnostic tests for ADR are usually absent and a rechallenge is rarely justified ethically. In practice few adverse reactions are 'certain' or 'unlikely'; most are somewhere in between these extremes, i.e. 'Possible' or 'Probable'. In an attempt to solve this problem many systems have been developed for a structured and harmonised assessment of causality but none of these systems have shown to produce a precise and reliable quantitative estimation of relationship. Nevertheless, causality assessment has become a common routine procedure in pharmacovigilance.

The AMC is responsible for performing causality assessment of reports which shall be reviewed at NCC. The PvPI follows WHO-UMC causality assessment scale for establishing the relation between the suspected drug and suspected adverse drug event. The WHO-UMC scale is used as a practical tool for the assessment of case reports. It is basically a combined assessment taking into account the clinical-pharmacological aspects of the case history and the quality of the documentation of the observation.

6.3 Advantages and Limitations of Standardised Case Causality Assessment

What causality assessment can do	What causality assessment cannot do
▪ Decrease disagreement between assessors ▪ Classify relationship likelihood ▪ Mark individual case reports ▪ Improvement of scientific evaluation	▪ Helps in differential diagnosis ▪ Distinguish valid from invalid cases ▪ Prove the connection between drug and event ▪ Quantify the contribution of a drug to the development of an adverse event ▪ Change uncertainty into certainty

6.4 WHO-UMC Causality Assessment Scale

Causality term	Assessment criteria
Certain	▪ Event or laboratory test abnormality, with plausible time relationship to drug intake ▪ Cannot be explained by disease or other drugs ▪ Response to withdrawal plausible (pharmacologically, pathologically) ▪ Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon) ▪ Rechallenge satisfactory, if necessary
Probable/ Likely	▪ Event or laboratory test abnormality, with reasonable time relationship to drug intake ▪ Unlikely to be attributed to disease or other drugs ▪ Response to withdrawal clinically reasonable ▪ Rechallenge not required
Possible	▪ Event or laboratory test abnormality, with reasonable time relationship to drug intake ▪ Could also be explained by disease or other drugs ▪ Information on drug withdrawal may be lacking or unclear
Unlikely	▪ Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) ▪ Disease or other drugs provide plausible explanations
Conditional/ Unclassified	▪ Event or laboratory test abnormality ▪ More data for proper assessment needed, or ▪ Additional data under examination
Unassessable/ Unclassifiable	▪ Report suggesting an adverse reaction ▪ Cannot be judged because information is insufficient or contradictory ▪ Data cannot be supplemented or verified

Chapter 7: Signal Detection and Evaluation

Signal detection and its clinical assessment is an important domain of pharmacovigilance. The WHO has defined a *Signal* as "Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously." Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information. In a broader approach a signal is an alert from any available data source that a drug may be associated with a previously unrecognized hazard or that a known hazard may be quantitatively (e.g. more frequent) or qualitatively (e.g. more serious) different from existing knowledge. It is worth mentioning that a signal does not imply causation but it can only provide preliminary information about postulating a hypothesis and not for testing it. Analysis of national pharmacovigilance database can be used for signal detection which would reviewed by Signal Review Panel to arrive at any conclusion and making the decisions on that respects. In the context of spontaneous ADR reporting, a signal is normally series of cases of similar suspected ADRs reported in relation to a particular drug. Three cases are generally considered to be the minimum number of cases needed.

Various methods have been used to detect signals using spontaneous reporting data. Based on different statistical methodology - either the *Bayesian* or *Frequentist* approach, the basic concept behind these method is measurement of disproportionality i.e. determination to what extent the number of observed cases differs from the number of expected cases. When all drugs are considered together, large ADR database tend to have fairly stable proportions of particular reaction over time. That proportion is used as a baseline for comparison- that is to determine what would be expected if there was no signal.

The WHO UMC uses the BCPNN – (Bayesian Confidence Propagation Neural Network) while US FDA uses the MGPS- (Multi item Gamma Poisson Shrinker) methodologies. Other disproportionality analyses methods are ROR (Reporting Odds Ratio), PRR (Proportional Reporting Ratio) are employed by some national reporting centres and drug safety research units.

In the BCPNN methodology computation of the Information Component (IC) is based on prior and posterior probabilities. As per the WHO-UMC, the IC measures the disproportionality in the reporting of a drug-ADR pair in an ICSR database, relative to the reporting expected based on

the overall reporting of the drug and the ADR. Positive IC values indicate higher reporting than expected one. However, review of signals generated by using such tools must be analysed by clinicians and drug safety experts before arriving at a conclusion.

Whichever method is used for signal detection, each has its advantages and disadvantages and therefore there is no single method which can be considered as the gold standard. Signal Review Panel under PvPI identifies and review the signals from the national database.

Chapter 8: PvPI and WHO-UMC Collaboration

In order to participate in International Drug Monitoring Programme, NCC-PvPI collaborates with WHO-UMC. The following software tools are provided by WHO-UMC to achieve the objectives of PvPI in a more efficient way.

8.1 VigiFlow

VigiFlow is a web-based ICSR management system that is specially designed for use by national centres in the WHO Programme for International Drug Monitoring. VigiFlow is based on and compliant with the ICH E2B standard and is a trademark of the UMC and maintained by the UMC in Uppsala, Sweden. It offers a simple, fast and secure web-based solution that improves all aspects of ADR reporting. ICSR data can be manually entered into VigiFlow with support from the latest versions of terminologies such as the WHO-DD and WHO-ART or MedDRA. Once a report is complete and committed the first version of the ICSR is generated and it will automatically saved in VigiBase (WHO Global ICSRs Database). It is easy to retrieve reports for amend the contents or add follow-up information.

8.2 VigiBase

VigiBase is the WHO global ICSR database; it consists of reports of adverse reactions received from member countries since 1968. The VigiBase data resource is the largest and most comprehensive in the world, and it is developed and maintained by the UMC on behalf of the WHO. The VigiBase database system includes linked databases containing medical and drug classifications: WHO-ART/MedDRA, WHO ICD, and WHO-DD. It is a computerised pharmacovigilance system, in which information is recorded in a structured, hierarchical form to allow for easy and flexible retrieval and analysis of the data. Its purpose is to provide the evidence from which potential medicine safety hazards may be detected.

8.3 VigiMine

VigiMine was launched in 2008 as a new development in VigiSearch. VigiMine gives access to statistical data on all drug-ADR pairs reported to VigiBase. VigiMine allows filtering of the

results on a number of statistical criteria, as well as stratification by age, sex, country, and year of reporting. VigiMine also shows the change in the statistical values over time.

VigiMine data can be used to compare with statistics in a national database, as well as being an independent aid in the detection of new signals of drug safety issues.

8.4 VigiMed

VigiMed is a web-based forum for those working at national centres in the WHO Programme to have easy access to safety concerns in other countries, to check regulatory status, and to expedite the sharing of drug information. VigiMed is part of the UMC collaboration portal, a web-based platform managed by the UMC.

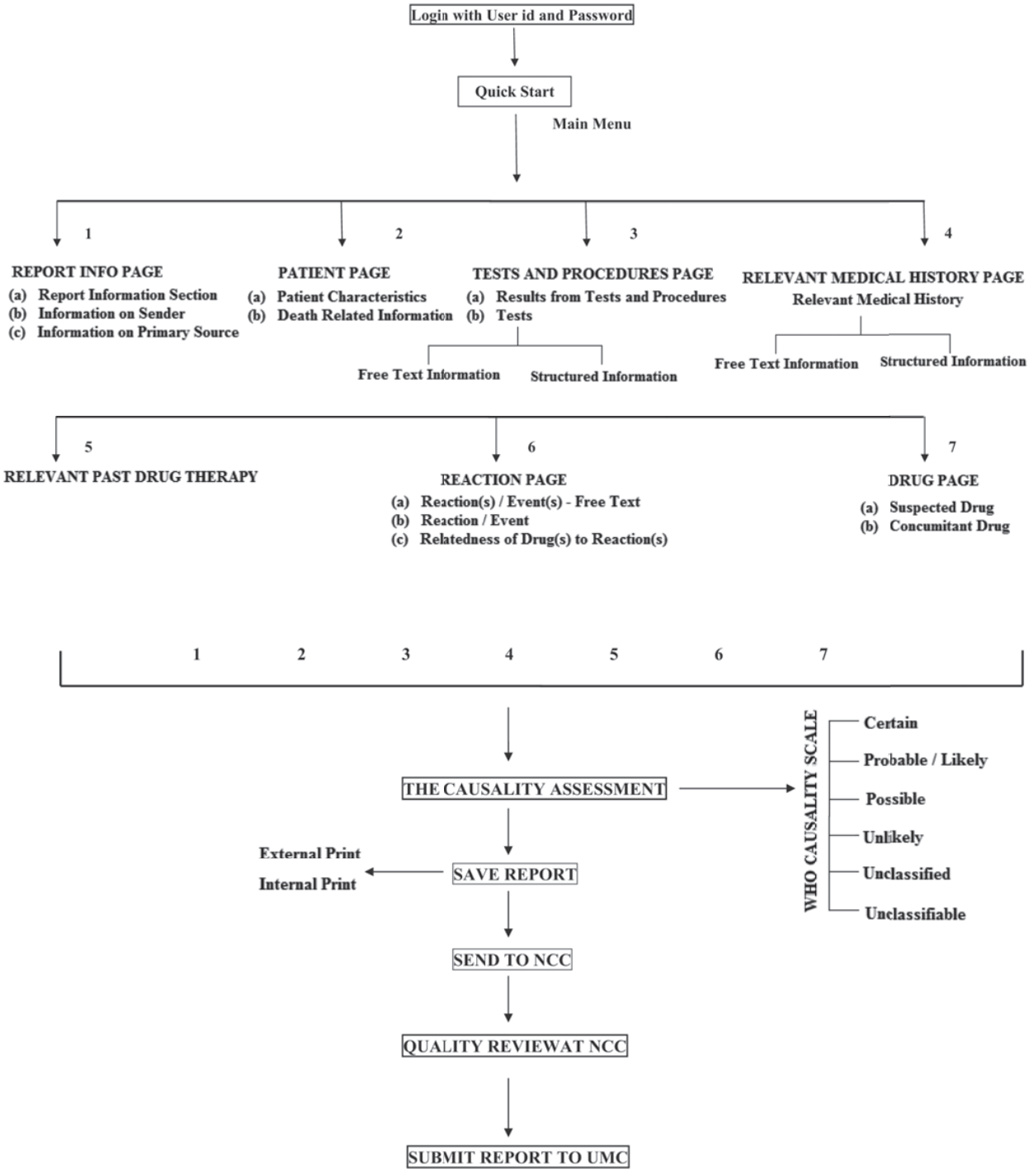
8.5 VigiSearch

VigiSearch is a powerful search tool that provides access to all case reports in VigiBase. VigiSearch allows for report searching across multiple drugs and ADRs simultaneously, as well as incorporating a range of filters. Drugs can be searched on a generic substance level or a specific trade name. VigiSearch also supports browsing the ATC structure. The results can be accessed on an overview level and viewed from a number of aspects (country, year, reaction term) or at the level of individual case report. For members of the WHO Programme, VigiSearch enables an international comparison of national spontaneous reporting data, as well as giving access to ADR information on drugs that are not yet on the national market.

8.6 VigiLyze

VigiLyze is a powerful search and analysis tool that provides access to more than 8 million ICSRs in VigiBase, submitted from over 100 countries. VigiLyze includes data on conventional medicines, traditional medicines as well as biological medicines including vaccines. VigiLyze can be used to have a global, regional or national view of an ADR identify or monitor international patient safety data. It can be useful to find supporting evidence while assessing Indian case reports or to see how Indian data support global pharmacovigilance. VigiLyze enables international comparison with national spontaneous reporting data, as well as giving access to ADR information on drugs that are not yet on our national market. Results from VigiLyze are instantly available as graphics as well as in tabular format.

8.7 VigiFlow-Demo Chart



Chapter 9: Risk Management, Communication and Publications

9.1 Risk Management

Risk management is the identification, assessment, and prioritization of risks followed by coordinated and economical application of resources to minimize, monitor, and control the probability and impact of unfortunate events. At the time of marketing authorisation, the benefit-risk balance is judged to be positive for the target population. A medicinal product is associated with multiple risks and individual risks will vary in terms of severity, effect on individual patient and public health impact. However, at the time when an initial authorisation is sought all the risks (actual or potential) have not been identified and many of the risks associated with the use of a medicinal product will only be discovered and characterised during post market authorisation.

Risk management has three stages which are inter-related as mentioned below:

1. Characterisation of the safety profile of the medicinal product including what is known and not known.
2. Planning of pharmacovigilance activities is to characterise and identify new risks and increase the knowledge in general about the safety profile of the medicinal product.
3. Planning and implementation of risk minimisation, mitigation and assessment of the effectiveness of these activities.

Risk management is a global activity. However the benefits and risk of a medicinal product may also vary amongst regions as they differ in disease prevalence, severity, population genetics (South Indian, North Indian, East Indian and West Indian). The overall aim of risk management is to ensure that the benefits of a particular medicinal product exceed the risks by the greatest achievable margin for the individual patient and for the target population as a whole.

9.2 Communication

Communicating safety information to patients and healthcare professionals is a public health responsibility and is essential for achieving the objectives of pharmacovigilance in terms of promoting the rational, safe and effective use of medicine, preventing harm from adverse reactions and contributing to the protection of public health. Communication in PvPI improves patient care, understanding, promotes transparency and accountability. All the communications

with WHO-UMC will be managed by NCC. The NCC is responsible to publish/communicate any findings from NCC database to journals/media/online-web whereas other stakeholders are required to get prior approval from NCC to publish/communicate any data or matter related to PvPI. Different modes of communications use in PvPI are as follow:

Press Communication

It includes press release and press briefings which are primarily intended for journalists. The Secretary-cum-Scientific Director, IPC or the designated person is the only authority to correspond with media, related to all activities of PvPI.

Website

A website is a key tool for the stakeholders including patients and health professionals. NCC and CDSCO shall ensure that all important safety information should be published on the websites under their control. (www.ipc.gov.in/PvPI/Pv_home.html)

Newsletter

To communicate the findings and regulatory status of medicine in India as well as globally to the stakeholders, IPC-NCC publishes newsletter i.e. "PvPI Newsletter" three issues in a year. This newsletter is for everyone concerned with the issues of pharmacovigilance which provides practical information and advice on drug safety and information about emerging safety issues. The newsletter can also be downloaded from IPC website www.ipc.gov.in or www.ipc.gov.in/PvPI/Pv_home.html

9.3 Publications

IPC publishes National Formulary of India which is a guidance document for promoting rational use of generic medicines.

Annexure 1: Contact details of AMC under PvPI

Healthcare Professionals are encouraged to report ADRs, if any, to the nearest AMC. The details of AMCs as follows:

S. No	State	Centre Name	Coordinator name	Email	Contact Number
1.	Andhra Pradesh	Andhra Medical College, King George Hospital (KGH), Jagadamba Area, KGH Down Rd, Maharanipeta, Visakhapatnam-530002	Dr. J. Sudha	prabhakar2202@gmail.com	09849903051
2.		Guntur Medical College, Kanna Vari Thota, Guntur-522004	Dr. Zaheda Bano	drzahedabano@gmail.com	094915834797/ 09849133268
3.		Peoples Education Society Institute of Medical Sciences and Research, Kuppam, Chittoor District-517425	Dr. P. Muralidhar	pharmacovigilancepesimsr@gmail.com	08331836915
4.		S. V. Medical College, Alipiri Road , Tirupati, Chittoor District-517507	Dr. Vasundhara Devi	vasuda61@yahoo.com	09849632862
5.		Kurnool Medical College, Budhawarpet, Kurnool-518002	Dr. Y. Vijaya Bhaskar Reddy	drvijayabhaskarareddy@gmail.com	09989502205
6.		Rajivgandhi Institute of Medical Sciences, Near Balaga, Srikakulam-532001	Dr. N. Indira Kumari	rif_srikakulam@yahoo.com	08942278112, 09701501067, 09849373568
7.	Assam	Govt. Medical College, Narakachal Hill Top, Guwahati-781032	Dr. Mangala Lahkar	dr_mlahkar@rediffmail.com	09864073346
8.		Silchar Medical College & Hospital, Ghungoor, Silchar-788014	Dr. Pinaki Chakravarty	dr_pinaki@yahoo.com	09957198505
9.		Jorhat Medical College & Hospital, Kushal Konwar Path, Barbheta, P.O. Jorhat-785001	Dr. Nilotpal Barua	pharmacologyjmch@gmail.com	09613860564
10.	Bihar	Indira Gandhi Institute of Medical Sciences, Bailey Road, Sheikhpura, Patna-800014	Prof. (Dr.) Harihar Dikshit	dikshithariharpatna@yahoo.co.in	09334106381
11.		All India Institute of Medical Sciences, Phulwari Sharif, Patna-801505	Prof. P.P. Gupta	drprempgupta@gmail.com	07763800139 09415210579
12.		Lord Buddha Koshi Medical College & Hospital, NH 107, Baijnathpur, Saharsa-852201	Dr. Akhilesh Kumar	sykalabs@yahoo.co.in	09431243204.
13.	Chhattisgarh	Pt. JNM Medical College, Jail Road, Raipur- 492001	Dr. Rajesh Hishikar	rhishikar@gmail.com	09424205700
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15.	Gujarat	SMT NHL Municipal Medical College, Ellise Bridge, Ahmedabad-380006	Dr. Supriya D. Malhotra	supriyadmalhotra@gmail.com	09727760262
16.		BJ Medical College, New Civil Hospital, Asarwa, Ahmedabad-380016	Dr. Mira K. Desai	desaimirak@yahoo.com	09825057107

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18.		Surat Municipal Institute of Medical Education & Research, Ring Road, Near Sahara Darwaja, Opposite Bombay Market, Umarwara, Bharat Nagar, Surat-395010	Dr. Sachendra K. Srivastava	sachendra5@rediffmail.com/ drarvindsingh@yahoo.com	09898464713
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20.		PDU Medical College, Civil Hospital Campus, Jam Nagar Road, Jam Nagar Road, Rajkot- 360001	Dr. Anil Singh	docanil71@yahoo.co.in	09426974679
21.		Gujarat Medical Education & Research Society Medical College, Gotri, Vadodara-390021	Dr. Prakash Bhabhor	drbhabhor@gmail.com deanmcgv@gmail.com	09925014449
22.		Pramukhswami Medical College & Shree Krishna Hospital, Gokal Nagar, Karamsad, Dist. Anand- 388325	Dr. Bharat Gajjar	bharatmg@charutarhealth.org	09537500302 02692-222130, Ext. -3515
23.		Government Medical College, Baroda, Anandpura, Vadodara-390001	Dr. Niyati A. Trivedi	deanmcbrd@gmail.com natrivedi@yahoo.com	0265-2421594
24.	**Haryana**	Medanta-The Medicity Sector-38, Gurgaon-122001	Dr. Himanshu Baweja	himanshu.baweja@medanta.org	09990942044
25.		Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak-124001	Dr. M.C. Gupta	dr_mcgupta@yahoo.co.in/ dr.mcgupta57@gmail.com	09896015035
26.		BPS GMC for women, Khanpur Kalan, Sonepat-131305	Dr. Seema Rani	Seema17march@gmail.com	09466359666
27.		Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala-133207	Dr. Rani walia	hod.pharmacology@mmumullana.org	09815551386
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29.		Indira Gandhi Medical College, Circular Rd, Lakkar Bazar, Shimla-171001	Dr. A.K. Sahai	drashoksahai@gmail.com	09418468582
30.	**J&K**	Govt. Medical College, Maheshpura Chownk, Bakshi Nagar, Jammu-180001	Dr. Vishal Tandon	dr_vishaltandon@yahoo.com	09419195126
31.		Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar-190011	Dr. Z.A. Wafai	drzawafai@gmail.com	09419011862
32.		Acharya Shri Chander College of Medical Sciences & Hospital, N.H. Bye pass, P.O. Majeen Sidhra-180017	Dr. Pavan Malhotra	ascomshospital@gmail.com	09419182264
33.		Govt. Medical College, Karan Nagar, Srinagar-190010	Dr. Zubair Ashai	zubairashai@yahoo.co.uk	09419467514
34.	**Jharkhand**	Rajendra Institute of Medical Sciences (RIMS), Bariatu, Ranchi-834009	Dr. Janardan Sharma	drsharmaj@gmail.com	09431175014

35.	**Karnataka**	Bangalore Medical College and Research Institute, Fort, K.R. Road, Bengaluru-560002	Dr. C. R. Jayanthi	bmccrj@gmail.com	09448292424
36.		Belgaum Institute of Medical Sciences, Dr. B.R. Ambedkar Road, Belgaum-590001	Dr. Pankaj Kumar Masare	pankajmasare@gmail.com	09035330070
37.		Bidar Institute of Medical Sciences, Bidar, Udgir Rd, Bidar- 585401	Dr. B.O. Hanumanthappa	drbohanumanthappa@yahoo.com	09822426638
38.		JSS Medical College Hospital, Sri Shivarathreeshwara Nagar, Mysore-570015	Dr. Parthasarathi G.	partha18@gmail.com	09845659585
39.		Karnataka Institute Of Medical Sciences, P. B Road, Vidyanagar, Hubli-580022	Dr. Dutta Tria	adrkmc@gmail.com	09902354622
40.		Kasturba medical College, Light House Hill Road, Manipal-575001	Dr. K. L. Bairy	kl.bairy@manipal.edu/klbairy@yahoo.com	09449208478
41.		Mandya Institute of Medical Sciences (MIMS), District Hospital Campus, Mandya-571401	Dr. Nagabushan	bushan123@rediffmail.com	09448063431
42.		SDS Tuberculosis Research Centre & Rajiv Gandhi Institute of Chest Disease, Someshwaranagar 1st Main Road, Bengaluru-560029	Dr. Shashidhar Buggi	shashidharbuggi@gmail.com/ director.rgicd@gmail.com	09448042579
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48.		SDM College of Medical Sciences & Hospital, Manjushree Nagar, Sattur, Dharwad-580009	Dr. Radhika M.S.	drradhika78@gmail.com	09844645405
49.	**Kerala**	Govt. Medical College, P.O- Kozhikode-673008	Dr. Ajitha. K.N.	kn.ajitha50@gmail.com	09447180783
50.		Govt. Medical College, Gandhinagar, Kottayam-686008	Dr. Ramani P.T.	adrpharmac.mck@gmail.com	09446593762
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58.		SAIMS Medical College, Ujjain Highway, Sanwer Road, Indore- 453111	Dr. Chhaya Goyal	chhayagl@gmail.com	09827221640
59.		NSCB Medical College, Medical College Colony, Jabalpur- 482003	Dr. K.K. Daryani	nscbmcjb@gmail.com	0761-2673644, 2673645, 2673646
60.		All India Institute of Medical Sciences, Saket Nagar, Bhopal- 462024	Dr. Ratinder Jhaj	rati.pharm@aiimsbhopal.edu.in	0755-2902620
61.	**Maharashtra**	BJ Medical College & Sassoon General Hospital, Jai Prakash Narayan Road, Near Pune Railway Station, Pune- 411001	B.B. Ghonghane	bbghonghane_bb@yahoo.com	09922925590
62.		Government Medical College & Hospital, Ajni Rd, Nagpur-440003	Dr. Ganesh N. Dakhle	smitaavanti@yahoo.co.in/ gndakhle@rediffmail.com	09850539353
63.		Grant medical college & Sir JJ Group of Hospital, JJ Marg, Off Jijabhoy Road, Byculla Mumbai- 400008	Dr. S. B. Patel	pharmac.gmc@gmail.com/ dr.sbpatel.gmc@gmail.com	09821286701
64.		Indira Gandhi Government Medical College, C.A. Road, Nagpur-440018	Dr. Vandana Avinash Badar	drvandanabadar@yahoo.co.in,/ am1_badar@yahoo.com	09960031486
65.		Lokmanya Tilak municipal Medical College & General Hospital, Dr. Babasaheb Ambedkar Road, Sion-400022	Dr. Sudhir R. Pawar	dr.sudhirpawar@gmail.com	09869111630
66.		Mahatma Gandhi Institute of Medical Sciences, Nagpur Sevagram, Nagpur-442012	Dr. Sushil Kumar Varma	sushil@mgims.ac.in/varmasushil9@gmail.com	09921418999
67.		MGM Medical College and Hospital, Kalamboli, Navi Mumbai- 410209	Dr. Y.A. Deshmukh	yadeshmukh@gmail.com	09867129210
68.		Pd. Dr. D.Y. Patil Medical College, Gaikwad Haraibhau Vinayan Rd, Pimpri, Chinchwad, Pune -411018	Dr. A.V. Tilak	abhijeet.tilak@yahoo.com	09226145484
69.		Seth GS Medical College & KEM Hospital, Acharya Donde Marg, Parel-400012	Dr. Urmila Thatte	pvpiitakem@gmail.com/ urmilathatte@gmail.com	09820198462
70.		Swami Ramanand Teerth Rural Govt Medical College, Ambajogai, Dist. Beed- 43151	Dr. V.M. Motghare	vm.motghare@gmail.com	09890384074
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73.		Government Medical College, Sangli District, Miraj-416410	Dr. Shraddha Milind Pore	Shraddha.pore7@gmail.com	09371126946
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76.	**Meghalaya**	North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences, Mawdiangdiang, Shillong-793018	Dr. Dhriti Kumar Brahma	dbdhriti168@gmail.com	09436766171
77.	**Odisha**	VSS Medical College, Burla, Sambalpur-768031	Dr. Sabita Mohapatra	adr.vssmc.pharma@gmail.com	09238607960
78.		M. K. C. G Medical College, Ganjam, Berhampur- 760004	Dr. Bandana Rath	drbandanarath@yahoo.co.in	09437980235
79.		SCB Medical College and Hospital, Manglabag, Cuttack-753007	Dr. Srikanta Mohanty	swayam_1984@yahoo.co.in/adr.scbmch@gmail.com/ drkaliprasad@yahoo.co.in	09437271809
80.		Hi-tech Medical College & Hospital, Health Park, Pandara, Bhubaneshwar-751025	Dr. Parbaty Panda	Parbaty.panda@gmail.com	09437304089 0674-2371407
81.	**Punjab**	Christian Medical College and Hospital, Brown Road, Ludhiana-141008	Dr. Dinesh Kumar Badyal	dineshbadyal@gmail.com	09815333776
82.		Dayanand Medical College and Hospital, Tagore Nagar, Civil Lines, Ludhiana-141001	Dr. Sandeep Kaushal	skaushal1@yahoo.co.in	09876635367
83.		Govt. Medical College Patiala, New Lal Bagh, Patiala-147001	Dr. Anita Gupta	gomcoitcell@yahoo.com	09872139567
84.		Sri Guru Ram Das Institute of Medical Sciences & Research, Grand Trunk Rd, Amritsar-143006	Dr. Rahat Kumar	sgrdimsar@rediffmail.com rahat_sharma66@yahoo.com	0183-2870200, 2870204
85.		Guru Gobind Singh Medical College & Hospital, Sadiq Road, Faridkot-151203	Dr. Kamlesh Kohli	kkpharmacology@rediffmail.com	09815499689
86.		Government Medical College, Circular Road, Amritsar-143001	Dr. Jaswant Rai	drjaswantrai@gmail.com	08146896878
87.	**Rajasthan**	Sardar Patel Medical College, SP Medical College Rd, Sardar Patel Colony, Bikaner- 334001	Dr. (Ms.) Kiran Barar	drkiranbarar@rediffmail.com/ kiranbarar06@gmail.com	09352004922
88.		SMS Medical College, Jawaharlal Nehru Marg, Jaipur-302004	Dr. Mukul Mathur	Mathur_mukul@rediffmail.com/ coordpvpimsjp@rediffmail.com	09414324182
89.		Geetanjali Medical College and Hospital, geetanjali Medicity, Hiran Magri Extn, Eklingpura Chouraha, Udaipur-313001	Dr. Jameela Tehshildar	dr.jameelatahesildar@yahoo.com	0929303666
90.		R.N.T Medical College Ambedkar Circle or Court Circle, SH 32, Bhopalpura, Udaipur-313001	Dr. Meena Atray	drmatray@yahoo.com	09784646478
91.		NIMS Medical College, NIMS University, Shobha Nagar, Jaipur-303121	Prof. Shobha Kulshreshtha	contact@nimsr.com	9799415000, 9799459000, 9799446000
92.		All India Institute of Medical Sciences, Basni Industrial Area Phase-2, Jodhpur-342005	Dr. Pramod Kumar Sharma	pramod309@gmail.com	0291-2740329, 2980149

93.	**Sikkim**	Sikkim Manipal Institute of Medical Sciences, Tadong, Gangtok-737102	Dr. Supratim Datta	supratimdoc@gmail.com	09434488126 08967828551
94.	**Tamil Nadu**	Christian Medical College, Thorapadi P. O., Vellore-632002	Dr. J.V. Peter	peterjohnvictor @yahoo.com.au	09944294769
95.		Govt. Kilpauk Medical College, Perambur Purasawalkam, Chennai-600010	Dr. C. Ramachandra Bhat	bhatcr@gmail.com	09843126800
96.		Madras Medical College, E.V.R Periyar Salai, Park Town, Chennai-600003	Dr. R. Nandini	pvpi.chennai@gmail.com	09884286987
97.		PSG Institute of Medical Sciences & Research, Anna Nagar, Coimbatore-641004	Dr. S. Ramalingam	drrampsg@gmail.com	09894618450
98.		SRM Medical College Hospital & Research Centre, kattankulathur, Kanchipuram-603203	Dr. Jamuna Rani	jrs_durai@yahoo.co.in	09840279010
99.		Sri Ramachandra Medical College and Research Institute, Porur, Chennai-600116	Dr. Chellathai David	pvpisrmc@gmail.com hod.pharmacology@sriramachandra.edu.in	09444622698
100.		Madurai Medical College, Alwarpuram, Madurai-625020	Dr. Sheik Davooth	drsheik.1960@gmail.com	09994026056
101.		Tirunelveli Medical College, Tirunelveli-627011	Dr. B. Meenakshi	meenakshi_b@tvmc.ac.in	09443496909
102.		Coimbatore Medical College & Hospital, Trichy Road, Gopalapuram, Coimbatore-641014	Dr. N. Shanthi	shanthisundarrajan@gmail.com	09443113740
103.	**Telangana**	Kakatiya Medical College, Rangampet Street, Warangal-506007	Dr. Raju Devde	rajudevde_dr@yahoo.co.in	09989125124
104.		Nizam Institute of Medical Sciences, Punjagutta Main Road, Hyderabad-500082	Dr. Shobha Udutha	shobhaudutha@gmail.com	09885235512
105.		Bhaskar Medical College & Bhaskar General Hospital, Yenkapally, Moinabad, Ranga Reddy-500075	Dr. G. Vijay Lakshmi	yadagirivijayalakshmi@yahoo.com	08413-235447
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107.		Gandhi Medical College, Musheerabad, Secundrabad-500003	Dr. T.S. Usha Shree	ushasreetakkella@yahoo.com	09848592058
108.		Osmania medical College, Koti, Hyderabad-50019	Dr. V. Prasanna	vprasanna@yahoo.com pharmacologyomc@gmail.com	09440359790
109.	**Tripura**	Agartala Govt. Medical College, Kunjaban, Agartala-799006	Dr. Debasis Ray	agmc@rediffmail.com	09436125100
110.		Tripura Medical College & Dr. Bram Teaching Hospitals, Hapania, Agartala-799014	Dr. T.N. Sarma	ghoshranjib@rediffmail.com	09436139660
111.	**Uttar Pradesh**	B.R.D Medical College & Nehru Hospital, Gorakhpur- 273013	Dr. Jamal Haider	jamal001@gmail.com	09839828358
112.		GSVM Medical College, Swaroop Nagar, Kanpur- 208001	Dr. S.P. Singh	singhdrsp@gmail.com	09415154744
113.		Institute of Medical Sciences Banaras Hindu University, Varanasi- 221005	Dr. B.L. Pandey	blp53@rediffmail.com	05422369711

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115.		M.L.B. Medical College, Jhansi- 284128	Dr. Sadhna Kaushik	kaushiksadhna55@gmail.com	07897038922
116.		M.L.N Medical College, Darbhanga Colony, George Town, Allahabad- 211002	Dr. Rakesh Chandra Chaurasia	drrakesh65@rediffmail.com	09415615064
117.		Santosh Medical University, Santosh Nagar, Ghaziabad-201001	Dr. V. C. Chopra	vipen.chopra@gmail.com	07838961411
118.		U.P Rural Institute of Medical Sciences and Research, Safai, Etawah-206130	Dr. Asha Pathak	drasha_pathak@yahoo.co.in	09451021779
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122.		Era's Lucknow Medical College & Hospital, Sarfazganj, Moosa Bagh picnic Spot, Hardoi Road, Lucknow-226003	Dr. Afroz Abidi	afrozabidi@gmail.com	09794979717
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129.		All India Institute of Medical sciences, Virbhadra road, Rishikesh-249201	Dr. Puneet Dhamija	drpdhamija@gmail.com	08475000292
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137.		College of Medicine & J.N.M. Hospital, Kalyani, Nadia-741235	Dr. Tirthankar Deb	principal.comjnmh.kalyani@gmail.com	033-25025564
138.		North Bengal Medical College, PO Sushrutanagar, Siliguri, Distt. Darjeeling-734012	Dr. Anupam Gupta	root@nbmc.wb.nic.in	0353-2581285, 2585512
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142.		Indraprastha Apollo Hospital Mathura Road, Sarita Vihar, New Delhi -110044	Dr. Lalit Kanodia	clinicalpharma@live.com	09650655660
143.		Lady Hardinge Medical College (LHMC), C 604, Shivaji Stadium Bus Terminal Co. Place Shaheed Bhagat Singh Marg, New Delhi-110001	Dr. H.S. Rehan	harmeetrehan@hotmail.com	09811694040
144.		University College of Medical Sciences, adjacent to GTB Hospital, Dilshad Garden, New Delhi -110095	Dr. S. K. Bhattacharya	skbnpl@yahoo.co.in	09811075825
145.		Vallabhbhai Patel Chest Institute (VPCI), University of Delhi, Guru Tegh Bhadur Road, New Delhi -110007	Prof. A. Ray	arunabha14@yahoo.co.in	09818037595
146.		VMMC & Safdarjung Hospital, Mahatma Gandhi Marg, Raj Nagar, Safdarjung, New Delhi – 110029	Dr. C.D. Tripathi	cdtripathi@gmail.com	09818665424
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148.		Maulana Azad Medical College and associated Lok Nayak, Govind Ballabh Pant Hospital & Guru Nanak Eye Centre, 2, B.S.Z. Marg, New Delhi -110002	Dr. Uma Tekur	umatekur@yahoo.com	09968604282
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Annexure 2: Terminologies used in Pharmacovigilance

Absolute risk

Risk in a population of exposed persons; the probability of an event affecting members of a particular population (e.g. 1 in 1,000). Absolute risk can be measured over time (incidence) or at a given time (prevalence).

Adverse event

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

Adverse (drug) reaction (ADR)

A response which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function (WHO, 1972).

An adverse drug reaction, contrary to an adverse event, is characterized by the suspicion of a causal relationship between the drug and the occurrence, i.e. judged as being at least possibly related to treatment by the reporting or a reviewing health professional.

Association

Events associated in time but not necessarily linked as cause and effect.

Attributable risk

Difference between the risk in an exposed population (absolute risk) and the risk in an unexposed population (reference risk). Also referred to as excess risk.

Attributable risk is the result of an absolute comparison between outcome frequency measurements, such as incidence.

Examples: If the exposed persons with a particular outcome are A, the exposed persons without the outcome are B, the unexposed persons with the outcome are C and the unexposed persons with the outcome are D, then the attributable risk is calculated as : [A / (A+B)] - [C / (C+D)]. If, during the same time period, the incidence of rash in a population treated with medicine X is

20/1,000=0.02, and the incidence of rash in a population not treated with X is 5/2,000=0.0025, the attributable risk is (20/1,000) - (5/2,000) = 0.0175.

Benefit

An estimated gain for an individual or a population. See also Effectiveness/Risk.

Benefit - risk analysis

Examination of the favourable (beneficial) and unfavourable results of undertaking a specific course of action. (While this phrase is still commonly used, the more logical pairings of benefit-harm and effectiveness-risk are slowly replacing it).

Biological products

Medical products prepared from biological material of human, animal or microbiologic origin (such as blood products, vaccines, insulin).

Causal relationship

A relationship between one phenomenon or event (A) and another (B) in which A precedes and causes B.In pharmacovigilance; a medicine causing an adverse reaction.

Causality assessment

The evaluation of the likelihood that a medicine was the causative agent of an observed adverse reaction. Causality assessment is usually made according established algorithms.

CIOMS

The Council for International Organizations of Medical Sciences (CIOMS) is a body set up under World Health Organization and UNESCO. It has developed a series of guidelines on pharmacovigilance, drawn up by a committee of volunteers from Industry, regulatory authorities, WHO and others.

The main guidelines concern the international reporting form (CIOMS I); periodic safety update reports (CIOMS II); core data sheets (CIOMS III); benefit-risk assessments (CIOMS IV); practical issues in pharmacovigilance (CIOMS V); clinical trial safety data (CIOMS VI); and development safety update reports (CIOMS VII).

Clinical trial

A systematic study on pharmaceutical products in human subjects (including patients and other volunteers) in order to discover or verify the effects of and/or identify any adverse reaction to

investigational products, and/or to study the absorption, distribution, metabolism and excretion of the products with the objective of ascertaining their efficacy and safety.

Cohort Event Monitoring

Cohort Event Monitoring (CEM) is a prospective, observational study of events that occur during the use of medicines, for intensified follow-up of selected medicinal products phase. Patients are monitored from the time they begin treatment, and for a defined period of time. See also Prescription Event Monitoring.

Common Epidemiology

In pharmacovigilance, an event with a frequency between 1 in 100 and 1 in 10.

Co-morbidities

Two or more coexisting medical conditions or disease processes that are additional to an initial diagnosis.

Compliance

Faithful adherence by the patient to the prescriber's instructions.

Congenital Anomalies

Morphological, functional and/or biochemical developmental disturbance in the embryo or foetus whether detected at birth or not. The term congenital anomaly is broad and includes congenital abnormalities, foetopathies, genetic diseases with early onset, developmental delay, etc.

Control group

The comparison group in drug-trials not being given the studied drug.

Critical terms

Some of the terms in WHO-ART are marked as "Critical Terms". These terms either refer to or might be indicative of serious disease states, and warrant special attention, because of their possible association with the risk of serious illness which may lead to more decisive action than reports on other terms.

Data-mining

Data mining is the process to analyse the data in different prospective & summerized it into useful information such as signal detection, benefit & risk analysis, etc.

Dechallenge

The withdrawal of a drug from a patient the point at which the continuity, reduction or disappearance of adverse effects may be observed.

Disproportionality analysis

Screening of ICSR databases for reporting rates which are higher than expected. For drug-ADR pairs, common measures of disproportionality are the Proportional Reporting Ratio (PRR), the Reporting Odds Ratio (ROR), The Information Component (IC), and the Empirical Bayes Geometrical Mean (EBGM). There are also disproportionality measures for drug-drug-ADR triplets, such as Omega (Ω).

Drug Abuse

It is a patterned use of a drug in which the user consumes the substance in amounts or with methods neither approved nor supervised by medical professionals.

Effectiveness/risk

The balance between the rate of effectiveness of a medicine versus the risk of harm is a quantitative assessment of the merit of a medicine used in routine clinical practice. Comparative information between therapies is most useful. This is more useful than the efficacy and hazard predictions from pre-marketing information that is limited and based on selected subjects.

Efficacy

The ability of a drug to produce the intended effect as determined by scientific methods, for example in pre-clinical research conditions (opposite of hazard).

Epidemiology

The science concerned with the study of the factors determining and influencing the frequency and distribution of disease, injury and other health-related events and their causes in a defined human population for the purpose of establishing programs to prevent and control their development and spread (Dorland's Illustrated Medical Dictionary).

Essential medicines

Essential medicines are those that satisfy the priority health care needs of the population. They

are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness.

EVMPD

The EudraVigilance Medicinal Product Dictionary (EVMPD) has been developed by the European Medicines Agency in collaboration with the EudraVigilance Joint Implementation Group. The main objective of the EVMPD is to assist the pharmacovigilance activities in the European Economic Area.

EUDRAGENE

Eudragene is a European collaboration that established a collection of DNA samples as a resource for studying genes which influence serious or adverse drug reactions (ADRs). Identifying genes that influence susceptibility to adverse reactions will advance understanding of the basis of adverse drug reactions and may also lead to the development of tests that can predict individual susceptibility to adverse reactions.

Excipients

All materials included to make a pharmaceutical formulation (e.g. a tablet) except the active drug substance(s).

Formulary

A listing of medicinal drugs with their uses, methods of administration, available dose forms, side effects, etc., sometimes including their formulas and methods of preparation.

Generic (multisource product)

The term "generic product" has somewhat different meanings in different jurisdictions. Generic products may be marketed either under the non-proprietary approved name or under a new brand (proprietary) name. They are usually intended to be interchangeable with the innovator product, which is usually manufactured without a license from the innovator company and marketed after the expiry of patent or other exclusivity rights.

Harm

The nature and extent of actual damage that could be caused by a drug. Not to be confused with risk.

ICH

The International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for human use.

ICD

International Classification of Diseases (ICD) is the standard diagnostic tool for epidemiology, health management and clinical purposes.

Incidence

The extent or rate of occurrence, especially the number of new cases of a disease in a population over a period of time.

Individual Case Safety Report

A report that contains information describing a suspected adverse drug reaction related to the administration of one or more medicinal products to an individual patient.

MedDRA

MedDRA or Medical Dictionary for Regulatory Activities is a clinically-validated international medical terminology used by regulatory authorities and the regulated biopharmaceutical industry. The terminology is used through the entire regulatory process, from pre-marketing to post-marketing, and for data entry, retrieval, evaluation, and presentation.

Medical error

An unintended act (either of omission or commission) or one that does not achieve its intended outcomes.

Over the counter (OTC)

Medicines which are available for purchase without prescription.

Off-label-use

When the medicinal product is intentionally used for a medical purpose not in accordance with the authorised product information.

Overdose

Administration of a quantity of a medicinal product given per administration or cumulatively,

which is above the maximum recommended dose according to the authorised product information.

Pharmacoepidemiology

Study of the use and effects of drugs in large populations.

Pharmacology

Pharmacology is the science of drugs (Greek: Pharmacon-drug; logos-discourse in) . In a broad sense, it deals with interaction of exogenously administered chemical molecules (drugs) with living systems. It encompasses all aspects of knowledge about drugs, but most importantly those that are relevant to effective and safe use for medicinal purposes.

Pharmacovigilance

The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

Phocomelia

The term comes from *Phaco* (seal) & *melia* (limb). It is a birth defect in which the hands & feet are attached to abbreviated arms & legs.

Placebo

An inactive substance (often called a sugar pill) given to a group being studied to compare results with the effects of the active drug.

Polypharmacy

The concomitant use of more than one drug, sometimes prescribed by different practitioners.

Post-authorization safety study (PASS)

A pharmacoepidemiological study or a clinical trial carried out in accordance with the terms of the Marketing Authorisation, with the aim of identifying or quantifying a safety hazard relating to an authorized medicinal product.

Post-marketing

The stage when a drug is generally available on the market.

Predisposing factors

Any aspect of the patient's history (other than the drug) which might explain reported adverse

events (for example, genetic factors, diet, alcohol consumption, disease history, polypharmacy or use of herbal medicines).

Pre-marketing

The stage before a drug is available for prescription or sale to the public.

Prescription event monitoring (PEM)

System created to monitor adverse drug events in a population. Prescribers are requested to report all events, regardless of whether they are suspected adverse events, for identified patients receiving a specified drug. Also more accurately named "cohort-event monitoring".

Prescription only medicine (POM)

Medicinal product available to the public only on prescription.

Prophylaxis

Prevention or protection.

PSUR

The Periodic Safety Update Report (PSUR) is a stand-alone document that allows a periodic but comprehensive assessment of the worldwide safety data of a marketed drug or biological product.

QPPV

Qualified Person responsible for Pharmacovigilance.

Rare

In pharmacovigilance an event with a probability between 1 in 10,000 and 1 in 1,000

Rational drug use

An ideal of therapeutic practice in which drugs are prescribed and used in exact accordance with the best understanding of their appropriateness for the indication and the particular patient, and of their benefit, harm effectiveness and risk.

Rechallenge

The point at which a drug is again given to a patient after its previous withdrawal (see dechallenge).

Reference risk

Risk in a population of unexposed persons. Also called baseline risk. Reference risk can be

measured over time (incidence) or at a given time (prevalence). The unexposed population refers to a reference population, as closely comparable to the exposed population as possible, apart from the exposure.

Regulatory authority

The legal authority in any country with the responsibility of regulating all matters relating to drugs.

Relative risk

Ratio of the risk in an exposed population (absolute risk) and the risk in an unexposed population (reference risk). Relative risk is the result of a relative comparison between outcome frequency measurements, e.g. incidences.

Example: If the exposed persons with an outcome are A, the exposed persons without the outcome are B, the unexposed persons with the outcome are C, and the unexposed persons without the outcome are D, the relative risk is calculated as [A / (A+B)] / [C / (C+D)].

If the incidence of rash in a population treated with medicine X is 35/1,500=0.023, and the incidence of rash in a population which is not treated with X, during the same time period, is 5/2,000=0.0025, the relative risk is (35/1,500) / (5/2,000) = 9.3.

Risk

The probability of harm being caused; the probability (chance, odds) of an occurrence

SAEC

The International Serious Adverse Events Consortium (SAEC) is a non-profit consortium formed in October 2007 between industry, academia, the Welcome Trust, and the US Food and Drug Administration to identify genetic variants associated with serious adverse events.

Serious Adverse Event or Reaction

A serious adverse event or reaction is any untoward medical occurrence that at any dose:

- results in death
- results in life-threatening condition
- requires inpatient hospitalization or prolongation of existing hospitalization

- results in persistent or significant disability/incapacity
- causes congenital abnormality
- requires any intervention to prevent the occurrence of any of the above

To ensure no confusion or misunderstanding of the difference between the terms "serious" and "severe", the following note of clarification is provided:

The term "severe" is not synonymous with serious. In the English language, "severe" is used to describe the intensity (severity) of a specific event (as in mild, moderate or severe); the event itself, however, may be of relatively minor medical significance (such as severe headache). Seriousness (not severity) which is based on patient/event outcome or action criteria serves as guide for defining regulatory reporting obligations.

Side effect

Any unintended effect of a pharmaceutical product occurring at normal dosage which is related to the pharmacological properties of the drug.

Signal

Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information. The publication of a signal usually implies the need for some kind of review or action.

Spontaneous reporting

System whereby case reports of adverse drug events are voluntarily submitted from health professionals and pharmaceutical manufacturers to the national regulatory authority.

SUSAR (Suspected Unexpected Serious Adverse Drug Reaction)

A serious adverse drug reaction whose nature, severity or frequency is not identified previously in the risk information provided to the clinical investigator's brochure (CIB) or on the drug label.

Summary of Product Characteristics

A regulatory document attached to the marketing authorization which forms the basis of the product information made available to prescribers and patients.

Teratogen

Environmental factors which can cause congenital abnormalities.

Traditional Medicines

Traditional medicine is the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness.

Uncommon

In pharmacovigilance an event with a frequency between 1 in 1,000 and 1 in 100.

Unexpected adverse reaction

An adverse reaction, the nature or severity of which is not consistent with domestic labeling or market authorization, or expected from characteristics of the drug.

VigiBase

The name of the WHO Global ICSR Database.

WHO-ART

Terminology for coding clinical information in relation to drug therapy. WHO-ART is maintained by UMC.

WHO Drug Dictionary (WHO-DD)

The WHO Drug Dictionary is an international classification of drugs providing proprietary and on-proprietary names of medicinal products used in different countries, together with all active ingredients.

Annexure 3: Organisations, societies, regulators and useful websites

1. The Central Drugs Standard Control Organisation Headquarters

CDSCO is the division of the Directorate General of Health Services, Government of India, and Ministry of Health & Family Welfare. It is headed by the Drug Controller General (India). The key functions of the organisation are to lay down the standards of drugs, cosmetics, diagnostics and devices; to lay down the regulatory measures, amendments to the Drugs & Cosmetic Act 1940 b and the Rules thereof; to regulate market authorization of new drugs; to regulate clinical research in India; to approve licences to manufacture certain categories of drugs as central licence approving authority for blood banks, large volume parenterals, vaccines and sera; to regulate import and standards of imported drugs; to do work relating to Drug Technical Advisory Board (DTAB) and Drug Consultative Committee (DCC), testing of drugs by Central Drugs laboratories. It also coordinates the functions of the State Drugs Control administration, screening of drugs formulations available in the country etc. Details of sub-zonal offices of the CDSCO and other functions of the organisation can be obtained from the website.

Official website: www.cdsco.nic.in

2. WHO Collaborating Centre for International Drug Monitoring:

The Uppsala Monitoring Centre

The WHO is a specialized agency of the United Nation that is concerned with international public health. The UMC is an independent foundation and a centre for international service and scientific research. UMC is a for-benefit foundation committed to innovative research and development in patient safety, and to provide data, tools, and consultation and training resources to health professionals all over the world. The World Health Organization set up its international drug monitoring programme after the thalidomide disaster. Since 1978 the WHO Programme for International Drug Monitoring has been carried out by Uppsala Monitoring Centre (UMC) in Sweden. UMC is the custodian and manager of VigiBase, the WHO global database of more than 8 million reports of adverse reactions to medicines

Official website: www.who-umc.org

3. WHO Country office for India

The WHO Country Office for India is headquartered in Delhi with country-wide presence. Its key aim is to improve health and equity in India. It distinguishes and addresses both the challenges to unleashing India's potential globally and the challenges to solve long-standing health and health service delivery problems internally. The WHO country office for India also coordinates with PvPI to organise pharmacovigilance training programs to its stakeholders.

Official website: www.whoindia.org

4. National Institute of Biologicals

National Institute of Biologicals is an autonomous institution under the MoHFW, Government of India and is a premier scientific organization and a centre of excellence to ensure quality of biologicals and vaccines in the country. The institute responsibly assures and reviews the quality of number of biological products available through domestic manufacturing or imports. The operations are carried out in the state of the art facility of the institute and in close coordination with regulatory authorities.

Official website: www.nib.gov.in

5. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use

ICH is a project that brings together the regulatory authorities and experts from pharmaceutical industry of Europe, Japan and United States to discuss scientific and technical aspects of pharmaceutical product registration.

Official website: www.ich.org

Annexure 4: Literature Resources for Pharmacovigilance

Following literature resources can provides further information to NCC and AMCs under PvPI, regarding drug safety monitoring and other aspects of pharmacovigilance.

Books

1. Bennett, P., Calman, K., Curtis, S. and Fischbacher-Smith, D. (2010) *Risk Communication and Public Health*, 2nd edition, Oxford University Press, USA.
2. CIOMS. (1999) *Benefit-Risk Balance for Marketed Drugs: Evaluating Safety Signals* (Report of CIOMS Working Group IV), WHO.
3. CIOMS. (2001) *Current Challenges in Pharmacovigilance: Pragmatic Approaches* (Report of CIOMS Working Group V), WHO.
4. CIOMS. (2010) *Practical Aspects of Signal Detection in Pharmacovigilance* (Report of CIOMS Working Group VIII), WHO.
5. Cobert, B. and Biron, P. (2008) *Practical Drug Safety from A to Z*, Jones & Bartlett Publishers.
6. Gupta, SK. (ed.) (2011) *Textbook of Pharmacovigilance*, Jaypee Brothers Medical Publishers (P) Ltd.
7. Mann, RD. and Andrews, EB. (ed.) (2007) *Pharmacovigilance*, 2nd edition, John Wiley & Sons Ltd.
8. MHRA. (2008) *Good Pharmacovigilance Practice Guide*, Pharmaceutical Press.
9. Van Boxtel, CJ.,Santoso, B. and Edwards, IR. (ed.) (2008) *Drug Benefits and Risks: International Textbook of Clinical Pharmacology*, 2nd edition, IOS Press.
10. Vincent, C. (2010) *Patient Safety*, 2nd edition, Wiley-Blackwell.
11. Waller, P. (2009) *An Introduction to Pharmacovigilance*, Wiley-Blackwell.

Journals/ Publications & Newsletters

1. A Lifetime in Safety - Selected articles by Ed Napke
2. A Practical Handbook on the Pharmacovigilance of Antimalarial Medicines
3. A Practical Handbook on the Pharmacovigilance of Antiretroviral Medicines
4. Accepted Scientific Names of Therapeutic Plants and their Synonyms
5. ADR Newsletters from National Centres
6. Aide Memoire - For a National Strategy for Safe Drugs and Their Appropriate Use
7. Being a Member of the WHO Programme
8. BMJ (British Medical Journal)
9. Dialogue in Pharmacovigilance - More Effective Communication
10. Drug Information Journal
11. Drug Safety
12. Effective Communications in Pharmacovigilance - The Erice Report
13. Expecting the Worst (2nd Edition 2010)
14. Indian Journal of Clinical Medicine
15. Indian Journal of Dentistry
16. Indian Journal of Dermatology
17. Indian Journal of Gastroenterology
18. Indian Journal of Health & Wellbeing
19. Indian Journal of Medicine
20. Indian Journal of Oncology & Radiation Biology
21. Indian Journal of Ophthalmology

22. Indian Journal of Pharmaceutical Sciences
23. Indian Journal of Pharmacology
24. Indian Journal of Pharmacy Practice
25. Indian Journal of Psychiatry
26. Indian Journal of Public Health
27. Indian Journal of Sexually Transmitted Diseases and AIDS
28. Indian Journal of Transfusion Medicine
29. JAMA (Journal of the American Medical Association)
30. Journal of Indian Medical Research
31. Pharmacoepidemiology & Drug Safety
32. Prescrire
33. Promoting Safety of Medicines for Children
34. PvPI Newsletters
35. Reactions Weekly
36. Safer Medicines, Safer Use of Medicines, Safer Patients (leaflet)
37. Safety Monitoring - Guidelines for Setting Up and Running a Pharmacovigilance Centre
38. Safety of Medicines - A Guide to Detecting and Reporting Adverse Drug Reactions
39. SIGNAL (Newsletter, UMC)
40. The Importance of Pharmacovigilance - Safety Monitoring of Medicinal Products
41. The Indian Journal of Hospital Pharmacy
42. The Indian Journal of Paediatrics
43. The International Journal of Risk & Safety in Medicine

44. The Journal of Family Welfare

45. The Lancet

46. The New England Journal of Medicine

47. The Nursing Journal of India

48. The Safety of Medicines in Public Health Programmes - Pharmacovigilance an Essential Tool

49. The world medicines situation 2011 Pharmacovigilance and safety of medicines

50. Uppsala Reports (News Bulletin)

51. WHO Drug Information

52. WHO Guidelines on Safety Monitoring of Herbal Medicines

53. WHO Pharmaceuticals Newsletter

54. WHO Policy Perspectives on Medicines no. 9 - PV: Ensuring the Safe Use of Medicines

55. WHO: Pharmaceuticals: Restrictions in Use and Availability

56. Writings on Pharmacovigilance - Selected articles by David J Finney

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