

# NATIONAL PHARMACOVIGILANCE PROTOCOL

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## PREAMBLE

India is a country of immense proportions. Its 3287590 sq. km. area, 1060 million population, 16 official languages and 35 states & union territories (several of which are larger than many European countries) don't lend themselves to conventional logistics. More than half a million qualified Doctors cater to the healthcare needs of our vast nation, supported by 6, 24000 beds in more than 15000 hospitals. Gigantic number of drugs are produced and consumed in India, which is the fourth largest producer of pharmaceuticals in the world.

Clearly aware of the enormity of task and determined to establish a vibrant, sustainable and credible adverse drug reaction monitoring programme in the country, the central drugs regulatory authority - the Central Drugs Standard Control Organization (CDSCO) - has initiated a well structured and highly participative National Pharmacovigilance Programme.

The National Pharmacovigilance Programme is largely based on the recommendations made in the WHO document titled "Safety Monitoring of Medicinal Products – Guidelines for Setting Up and Running a Pharmacovigilance Centre". The Programme aims to foster the culture of ADE notification in its first year of operation and subsequently aims to:

- generate broad based ADR data on the Indian population and share the information with global health-care community through WHO-UMC
- ensure optimum safety of drug products in the Indian market
- provide technical expertise for evaluating statutory AE reports furnished by sponsors conducting clinical trials in India

Even though India started participating in the WHO Pharmacovigilance programme many years ago and has several professionals who have organized many pharmacovigilance workshops, adverse drug reaction monitoring in India is still in its infancy.

An objective analysis of the earlier ADR monitoring attempts in India pointed towards deficiencies in attitude, expertise and management that included lack of reporting culture among physicians, lack of appropriate monitoring and supervision facility, lack of trained clinical pharmacists and nurses, as major factors. Further, health care professionals were not clear about what to report, how to report or where to report.

Over the last three years, CDSCO engaged various stake holders (Doctors, pharmacy professionals from hospitals, pharmaceutical industry, clinical research organizations as well as academicians from related fields) to discuss pharmacovigilance in Indian context and elicit suggestions for conceptualizing a robust nation-wide pharmacovigilance programme for generating, collating, analyzing and evaluating the data.

Two extensively participated discussion meetings, beginning from Mysore meeting in 2001, culminated in a workshop organized at Mumbai in March 2003, where a National Pharmacovigilance Protocol was documented, which now forms the bed-rock of the National Pharmacovigilance Programme in India.

The following professionals from across the country (listed in alphabetic order), representing the entire cross-section of stakeholders i.e. clinicians, medical academicians, drug regulators, pharmaceutical industry, pharmacists and pharmacologists participated at the momentous Mumbai meeting to evolve this consensual protocol:

Mr. Brijesh Regal (Protocol Coordinator),  
Dr. B Prabha Rao,  
Dr. Dilip Pawar,  
Dr. Ganesh Kadhe,  
Prof. K. C. Singhal,  
Dr. K. Rai,  
Dr. Meena Shrivastava,  
Mr. Moin Don,  
Prof. M.U.R. Naidu,  
Prof. P. Pandla,  
Mr. Raj Vaidya,  
Prof. S. D. Rajendran,  
Dr. (Mrs.) Rajsekharan,  
Prof. Ray,  
Prof. S. K. Sharma,  
Prof. S.K. Gupta,  
Dr. Sandeep Bandekar,  
Dr. Santanu Kumar Tripathi,  
Dr. Shobha Rani,  
Ms. Sunitha Srinivas,  
Dr. Urmila Thatte,  
Dr. Vasant V Joshi &  
Dr. Y.K. Gupta.

To effectively deal with the expected scale of operations in the country, National Pharmacovigilance Programme envisages several Peripheral Pharmacovigilance Centers pooling their data at five Regional Pharmacovigilance Centers which in turn funnel their data to the two Zonal Pharmacovigilance Centers.

Zonal Pharmacovigilance Centers are expected to analyze the data and submit consolidated information to the National Pharmacovigilance Centre where National Pharmacovigilance Advisory Committee would evaluate the data and recommends appropriate regulatory interventions.

# 1. BASICS OF PHARMACOVIGILANCE AND THE GLOSSARY OF TERMS

## 1a. Glossary of terms

### **National Pharmacovigilance Programme (NPP)**

The nation wide programme, sponsored and coordinated by the country's central drug regulatory agency – Central Drugs Standard Control Organization (CDSCO) – to establish and manage a data base of Adverse Drug Reactions (ADR) for making informed regulatory decisions regarding marketing authorisation of drugs in India for ensuring safety of drugs.

### **Peripheral Pharmacovigilance Centres (PPC)**

Primary pharmacovigilance centres. Relatively smaller medical institutions including individual medical practitioners' clinics, private hospitals, nursing homes, pharmacies etc.

First contact ADR data collection unit at a health care facility. They would be identified and coordinated by RPCs / ZPCs in consultation with CDSCO.

### **Regional Pharmacovigilance Centres (RPC)**

Secondary pharmacovigilance centres. Relatively larger healthcare facilities attached with medical colleges. They would act as second level centres in the administrative structure of the NPPI. They will function as first contact ADE data collection units also. They would be identified and coordinated by ZPCs in consultation with the CDSCO.

### **Zonal Pharmacovigilance Centre (ZPCs)**

Tertiary pharmacovigilance centres.

Large healthcare facilities attached with medical colleges in metro cities identified by the CDSCO for the purpose. They would act as third level centres in the administrative structure of the NPPI.

They will function as First contact ADE data collection units also.

### **Coordinator**

Designated in-charge of a particular participating PVig centre

### **Investigator**

A healthcare professional involved in investigation of drug related adverse events.

### **Notifier**

Any person who suspects to have experienced / observed an ADE and informs any participating Pharmacovigilance centre about it.

### **Reporter**

A healthcare professional reporting ADE on the ADE form.

### **Monitoring**

The process of overseeing drug related adverse events at the PVigC participating in the PVig Programme.

### **Reporting**

The process of providing ADR information by filling in the ADR form appropriately and forwarding the same to the appropriate level.

**Notification**

Process of informing by a notifier to any participating pharmacovigilance centre about the occurrence of a suspected ADE. The process may involve informing over telephone, in person, email, fax or any other means of communication-verbal or written.

All notifiers must give their contact details.

Appropriate and adequate measures must be taken to keep track of the notifier. Any follow up action will be initiated on a notification only after the due verification of the notifier. If the notifier cannot be traced back, it will be recorded on the notification slip before closing the case.

**Notification slip**

A pre-designed structured form made available by the NPPI for written communication of a suspected ADE by the notifier duly signed by him/her wherever feasible.

**ADR Form**

It's the pre-designed structured form issued by NPPI to record ADE.

**Archiving**

This is to be done at the Regional / Zonal Centres for a period of 5 years

**Audit**

A systematic and independent examination (conducted by personnel, independent of the centre) of centre's activities and documents to determine whether centre's activities were conducted and the data were recorded, analysed and accurately reported according to the protocol and \_\_\_\_ regarding performance of pharmacovigilance centre's participation in national pharmacovigilance programme.

**Causality Assessment**

See Section at the end of this proposal\*\*

**Confidentiality**

In a confidential / secretive manner.

**Side Effect**

Any unintended effect of a pharmaceutical product occurring at doses normally used in man which is related to the pharmacological properties of the drug.

*Comment: This is an old term and is broad enough to include both positive and negative effects of a drug apart from its main properties or indications. Some use the term as synonymous with 'adverse reaction', but the proposed definition will improve clarity of use of this term.*

**Adverse Event / Adverse Experience**

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.

*Comment: This is a more recent term which some use interchangeably with 'adverse reaction', but, as indicated, it is better reserved for clinical phenomena occurring during drug treatment where causality cannot be or is not ascertained.*

## **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.

*Comment: This describes the first alert of a problem with a drug. By its nature a signal cannot be regarded as definitive but indicates the need for further enquiry or action. On the other hand it is prudent to avoid a multiplicity of signals based on single case reports since follow up of all such would be impractical and time consuming. The definition allows for some flexibility in approach to a signal based on the characteristics of individual problems. Some would like a 'signal' to include new information on positive drug effects, but this is outside the scope of a drug safety Programme.*

## **Adverse Reaction**

WHO Technical Report No 498 (1972); 'A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.

*Comment: This basic definition includes all doses prescribed clinically, but is intended to exclude accidental or deliberate overdose. The sub classification of 'unexpected' was included to facilitate understanding of the type of adverse reaction which is most important to report to drug monitoring agencies.*

## **Unexpected Adverse Reaction**

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

## **Serious Adverse Event or Reaction**

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

- results in death
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- is life-threatening

*To avoid any 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. '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.*

## 1b. Most common types of adverse effects

### **Type A adverse effects** ('drug actions'):

pharmacological adverse effects

- Common (>1%)
- Dose relationship
- Suggestive time relationship
- Reproducible

**occurring in special situations** or patients with increased susceptibility

- Organ selective injury
- Late effects
- carcinogenicity, mutagenicity
- Interactions
- Risk situations:
  - childhood
  - the elderly
  - renal failure
  - haemodialysis
  - pregnancy
  - lactation

### **Type B adverse effects** ('patient reactions')

Immunoallergic reactions

- Metabolic intolerance
- Idiosyncrasy
- rare (<1%)
- unexpected
- causality uncertain
- mechanism uncertain
- no dose relationship
- not reproducible experimentally
- characteristic, serious
- suggestive time relationship
- low background frequency

### **Type C adverse effects** ('statistical effects')

Increased frequency of 'spontaneous' disease

- High background frequency
- Less typical for a drug reaction
- No suggestive time relationship
- Often long latency
- Mechanism unknown
- Difficult to reproduce experimentally

## 1. Commonly used Causality Assessment terms

### **Certain**

A clinical event, including laboratory test abnormality, occurring in a plausible time relationship to drug administration, and which cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge) should be clinically plausible. The event must be definitive pharmacologically or phenomenologically, using a satisfactory rechallenge procedure if necessary.

*Comment: It is recognized that this stringent definition will lead to very few reports meeting the criteria, but this is useful because of the special value of such reports. It is considered that time relationships between drug administration and the onset and course of the adverse event are important in causality analysis. So also is the consideration of confounding features, but due weight must be placed on the known pharmacological and other characteristics of the drug product being considered. Some times the clinical phenomena described will also be sufficiently specific to allow a confident causality assessment in the absence of confounding features and with appropriate time relationships, e.g. penicillin anaphylaxis.*

### **Probable / Likely**

A clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, unlikely to be attributed to concurrent disease or other drugs or chemicals, and which follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfil this definition.

*Comment: This definition has less stringent wording than for 'certain' and does not necessitate prior knowledge of drug characteristics or clinical adverse reaction phenomena. As stated no rechallenge information is needed, but confounding drug administration underlying disease must be absent.*

### **Possible**

A clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, but which could also be explained by concurrent disease or other drugs or chemicals. Information on drug withdrawal may be lacking or unclear.

*Comment: This is the definition to be used when drug causality is one of other possible causes for the described clinical event.*

### **Unlikely**

A clinical event, including laboratory test abnormality, with a temporal relationship to drug administration which makes a causal relationship improbable, and in which other drugs, chemicals or underlying disease provide plausible explanations.

*Comment: This definition is intended to be used when the exclusion of drug causality of a clinical event seems most plausible.*

### **Conditional / Unclassified**

A clinical event, including laboratory test abnormality, reported as an adverse reaction, about which more data is essential for a proper assessment or the additional data are under examination.

### **Unassessible / Unclassifiable**

A report suggesting an adverse reaction, which cannot be judged because information is insufficient or contradictory, and which cannot be supplemented or verified.

## Causality Assessment

Various causality terms are in use but the following are used most widely. Some, however, do not use all the terms, for instance many do not believe that a 'certain' classification is possible for a single report and other make no distinction between 'probable' and 'possible'. These definitions are however acceptable to Programme members who do use the terms. Where only 'possible' or 'unlikely' are used to describe reactions it must be understood that 'possible' include those reactions which are called by others 'probable' and 'certain', as well as 'possible'.

Whilst 'conditional/unclassified' and 'unassessable/unclassifiable' are not causality terms, they describe the status of adverse reaction reports and therefore allow for practical communication about ADR issues.

## Frequency of adverse drug reactions

*Whenever possible, an estimate of frequency should be provided, expressed in standard category of frequency.*

It is always difficult to estimate incidence on the basis of spontaneous reports, owing to the uncertainty inherent in estimating the denominator and degree of under-reporting. However, whenever possible, an estimate of frequency should be provided and in a standard form.

The following standard categories of frequency are recommended:

<i>Very common</i>	$\geq 1/10$	( $\geq 10\%$ )
<i>Common (frequent)</i>	$\geq 1/100$ and $< 1/10$	( $\geq 1\%$ and $< 10\%$ )
<i>Uncommon (infrequent)</i>	$\geq 1/1,000$ and $< 1/100$	( $\geq 0.1\%$ and $< 1\%$ )
<i>Rare</i>	$\geq 1/10,000$ and $< 1,000$	( $\geq 0.01\%$ and $< 0.1\%$ )
<i>Very rare</i>	$< 1/10,000$	(< 0.01%)

Precise rates will inevitably be based on studies and limited to the more common reactions. For reactions that are fewer than 'common', estimates of frequency will inevitably be based on spontaneous reports or on very large post-marketing studies or other special studies, and the numbers will be less precise; therefore, the source of the estimates (spontaneous or clinical) should be indicated. Stating the absolute numbers of cases reported may be misleading since they inevitably will become outdated.

## 2. NATIONAL PHARMACOVIGILANCE ADVISORY COMMITTEE

The National Pharmacovigilance Advisory Committee (NPAC) will oversee the performance of various Zonal, Regional and Peripheral Centres and will perform the functions of "Review Committee" for this program. The NPAC will also recommend possible regulatory measures based on pharmacovigilance data received from various centres. The composition of the NPAC is as under:

Chairperson	Director General Health Services
Member Secretary	DCG(I)
1. ICMR	D. G., ICMR, New Delhi
2. AIIMS, New Delhi, Zonal Centre Coordinator	Dr. S. K. Gupta, Head of the Department of Pharmacology, AIIMS, New Delhi
3. SGC Medical College, Mumbai, Zonal Centre Coordinator	Dr. Nilima Kshirsagar, SGS Medical College (Mumbai)
4. Member, Pharmacology	Dr. Ranjit Roy Choudhary, NII, New Delhi Dr. C. Adithan, Prof. Pharmacology JIPMER, Pondicherry
5. Forensic Medicine	Dr. T. D. Dogra, (AIIMS, New Delhi)
6. General Medicine	Dr. A. K. Agarwal (RML, New Delhi) Dr. Anoop Mishra (AIIMS, New Delhi)
7. Clinical Pharmacology	Dr. S. D. Seth, Chair-in Clinical Pharmacology (ICMR, New Delhi)
8. Member, Pharmacy	Mr. Brijesh Regal, WHO Consultant, New Delhi
9. Member, Toxicology	Dr. Y. K. Gupta, Director, (ITRC, Lucknow)
10. Member, Epidemiology	Dr. M. D. Gupte (ICMR Institute of Epidemiology, Chennai)
11. Member, Pathology	Dr. Kusum Verma Member Secretary, (AIIMS Ethics Committee, New Delhi)
12. Member, Drug Information	Dr. Pramil Tiwari (NIPER, Mohali)
13. Member, Phytotherapy	Dr. Urmila Thatte, Head of the Department of Pharmacology, B. L. Nair Medical College Hospital, Mumbai

### **3. NATIONAL PHARMACOVIGILANCE POLICY & MILESTONES**

#### **NATIONAL PHARMACOVIGILANCE POLICY**

Statement under the National Pharmacovigilance Programme of Government of India.

Since there are considerable social and economic consequences of adverse drug reactions and the positive benefit/cost ratio of implementing appropriate risk management – there is a need to engage health-care professionals and the public at large, in a well structured programme to build synergies for monitoring adverse drug reactions.

The purpose of the programme is to collate data, analyse it and use the inferences to recommend informed regulatory interventions, besides communicating risks to healthcare professionals and the public.

The National Pharmacovigilance Programme will have the following milestones:

- Short-term objectives: To foster a culture of notification
- Medium-term objectives: To engage several healthcare professionals and NGOs in the drug monitoring and information dissemination processes.
- Long-term objectives: To achieve such operational efficiencies that would make Indian National Pharmacovigilance Programme a benchmark for global drug monitoring endeavours.

#### **4. NATIONAL PHARMACOVIGILANCE PROGRAMME**

Before a product is marketed, experience of its safety and efficacy is limited to its use in clinical trials, which are not reflective of practice conditions as they are limited by the patient numbers and duration of trial as well as by the highly controlled conditions in which Clinical Trials are conducted.

The conditions under which patients are studied during the pre-marketing phase do not necessarily reflect the way the medicine will be used in the hospital or in general practice once it is marketed. Information about rare but serious adverse drug reactions, chronic toxicity, use in special groups (e.g. pregnant women, children, elderly) and drug interactions is often incomplete or not available. Certain adverse drug reactions may not be detected until a very large number of people have received the medicine.

**Pharmacovigilance is therefore one of the important post-marketing tools in ensuring the safety of pharmaceutical and related health products.**

Pharmacovigilance is defined as the detection, assessment and prevention of adverse drug reactions in humans.

It is the process of:

- Monitoring medicines as used in everyday practice to identify previously unrecognised adverse effects or changes in the patterns of their adverse effects
- Assessing the risks and benefits of medicines in order to determine what action, if any, is necessary to improve their safe use
- Providing information to users to optimise safe and effective use of medicines
- Monitoring the impact of any action taken

#### **5. FRAMEWORK FOR PHARMACOVIGILANCE IN INDIA**

The Central Drugs Standard Control Organization (CDSCO) is initiating a country-wide Pharmacovigilance programme under the aegis of DGHS, Ministry of Health & Family Welfare, Government of India.

The programme shall be coordinated by the National Pharmacovigilance Centre at CDSCO. The National Centre will operate under the supervision of the National Pharmacovigilance Advisory Committee to recommend procedures and guidelines for regulatory interventions.

#### **6. THE NATIONAL PHARMACOVIGILANCE CENTRE AT CDSCO**

**The National Pharmacovigilance Centre shall be based at CDSCO and:**

1. Shall monitor the adverse drug reactions of medicines in order to identify previously unexpected adverse drug reactions or indicate that certain reactions occur more commonly than previously believed. This will include the collation, review and evaluation of all spontaneous ADR reports received by the unit on a nation-wide basis. This information will then be keyed into the ADR database for use in aggregate analysis. These reports shall also be submitted to the WHO International Drug Monitoring Programme for international collaboration on drug safety.
2. Shall review Periodic Safety Update Reports (PSURs) submitted by pharmaceutical companies. Pharmaceutical companies are required to submit the PSURs of all

new chemicals drugs. PSURs shall be expected to be submitted every 6 monthly for the first 2 years of marketing in India, and annually for the subsequent 2 years.

3. Shall maintain contacts with international regulatory bodies working in pharmacovigilance and exchange information on drug safety.
4. Shall assess the regulatory information relating to safety in order to determine what action, if necessary, needs to be taken to improve safe use. Based on the available data, the Advisory Committee shall make recommendations on product label amendments, product withdrawals and suspension.
5. Shall provide information to end-users through adverse drug reaction news bulletins, drug alerts and seminars.

For further information please contact:  
The National Pharmacovigilance Centre  
Office of Drugs Controller General of India,  
Central Drugs Standard Control Organisation,  
Room No. 347-A,  
D.G.H.S., Ministry of Health & Family Welfare  
Nirman Bhawan, New Delhi 110 011.

Tel: (11) 23018806 Fax: (11) 23012648  
Email: dci@nb.nic.in www.cdsc.nic.in

## 7. OUTLINE OF THE NATIONAL PHARMACOVIGILANCE PROGRAMME

The National Pharmacovigilance Programme aims to provide adverse drug reaction data related to various drugs available in the country to the central drugs regulatory authority i.e. CDSCO. The programme will be coordinated by the National Pharmacovigilance Advisory Committee [NPAC] constituted by the Ministry of Health & Family Welfare. The Programme would comprise of the following steps:

**Step 1: Identifying various centres** across the country for capturing ADR related data

- a. Set-up 2 **Zonal Pharmacovigilance Centres** [ZPC] to coordinate the nationwide programme. [AIIMS for North and East and KEM-Mumbai for South and West]. Zonal Centres shall provide a room and other requisite infrastructure, e.g. a PC with internet facility, access to fax, telecom, etc.
- b. Identify 5 **Regional Pharmacovigilance Centres** [RPC] across the country
  - i. Ideally medical colleges with interested and initiated pharmacologists
  - ii. Can provide a small area (approx. 100 sq. feet)
  - iii. Can deploy a pharmacologist for the Programme
- c. Identify **Peripheral Pharmacovigilance Centres** [PPC]: *At least one teaching hospital in each state and union-territory*, and some other leading medical institutions, clinics or pharmacies in the area under each RPC .

- i. Ideally, centres that have internet facility
- ii. Manned by doctors / pharmacists who are enthusiastic about carrying out research activities e.g. monitoring ADRs
- iii. Visited by not less than a total of 50 patients daily in any/all of the following departments: Medicine, Gynecology, Pediatrics, Orthopedics, Cardiology, Oncology.

RPCs will also perform the functions of PPCs. Similarly ZPCs will also perform the function of PPCs.

All centres will have access to internets and Emails.

## **Step 2: Training and Coordination**

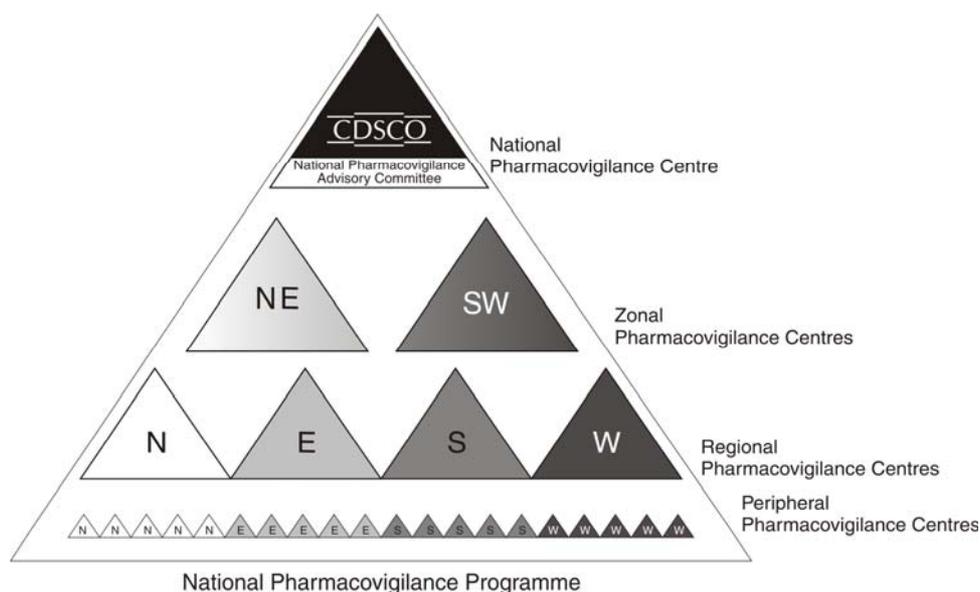
To ensure harmonized implementation of the Programme efforts shall be made to arrive at a uniform understanding of the operational systems, along with standardized formats to document and analyse ADRs. An induction training programme shall be arranged for healthcare professionals participating in the NPP.

Intensive interaction / training sessions will be organized for all participants to:

- i. Clearly define their individual and team roles and responsibilities
- ii. Set operational benchmarks e.g.
  - 1. Each PPC to record at least 30 AEs each month (statistically speaking 30 AEs in about 1500 patients who visit each month would be quite easy to record). Completed AE forms shall be forwarded to the concerned RPC at the end of each month.
  - 2. Each RPC
    - a. to collate and scrutinize the data received
    - b. to perform the causality analysis of all 120 to 150 forms received every month.
    - c. to submit a monthly report – prepared in a specific form to be forwarded to National Pharmacovigilance Centre (NPC) every month.
    - d. to report any alarming or critical ADRs to NPC along with supporting evidence.
  - 3. Each ZPC
    - a. to collate the data (approx. 1000-1200 forms) received from RPCs.
    - b. to verify / validate the causality analysis.
    - c. to prepare MIS reports for NPC in a specified format.
    - d. to pass on the final data to WHO Uppsala Centre for their global data pool.
    - e. to publish a periodic newsletter.
- iii. Evolve SOPs for generating and forwarding ADR data and for general conduct of the Programme (Zonal centres to prepare SOPs which must ensure that the Programme is conducted in compliance with this Protocol).
- iv. Impart relevant skills for carrying out ADR data capture namely

1. appropriate communication skills to elicit ADR related information
2. for recording ADR information through hands-on training
3. for meticulous collation and completeness of data
4. for fostering notification culture.

These training programs and interaction meetings shall be held every 6 months after the initial training. Besides, continuous communication through emails, carrying relevant information related to ADR monitoring methods shall be maintained among the participating centres.



**Hierarchical Structure of the Proposed Centres**

### **Broad objectives of the Programme**

- To foster the culture of AE notification and reporting
- To establish a viable and broad-based ADR monitoring program in India

### **Specific objectives of the Programme**

- To create an ADR database for the Indian population
- To create awareness of ADR monitoring among people
- To ensure optimum safety of drug products in Indian market
- To create infrastructure for ongoing regulatory review of PSURs

### **Coordinator's eligibility at different tiers of NPP**

- PPC – Any physician (primary-care or specialist), pharmacist
- RPC – A pharmacologist, preferably not below the rank of an assistant professor, attached to a medical college
- ZPC – A pharmacologist, not below the rank of a professor, attached to a medical college

All coordinators must obtain official permission, in writing; from their respective head of the institution / chief of the hospital, and submit the document to the NPC.

ZPCs will appoint dedicated pharmacologist and data managers (project staff). The pharmacologist must be computer literate. The data manager must have, sufficient competence in database designing, data entry and data analysis.

**Study population:**

Anyone experiencing adverse events suspected to be caused by drugs.

**Causality Assessment:**

As per WHO recommended methodologies.

**Archiving:**

All data generated (including reporting forms) will be stored and preserved for the purpose of archiving for a minimum period of 5 years, at the ZPCs.

**Confidentiality:**

Patient's identity is not revealed on the form – only the patient identifier is mentioned. Identity of the patients and related data will be used only for research and regulatory purpose and sufficient measures will be taken to maintain confidentiality of such information.

The identity of the notifier / reporter must be recorded in the AE form or Notification Slip so that in future the data can be verified if needed in future.

**Audit and Monitoring:**

Overall supervision of participating centres of all levels will be done by NPAC, through zonal offices as per a pre-designed audit protocol, thereby making room for prompt correction of deficiencies so detected. The purpose of the audit activities will be to ensure the quality of AE information, which must be authentic (including traceability of the patient), complete (all essential data elements filled-in), timeline compliant, and legible. The audit activity will also look into overall compliance with SOPs. The overall cost effectiveness analysis of the Programme will also be evaluated by the audit process. This would refer to regularity of the key personnel, particularly the dedicated Programme staff, and the average time they devote in the project work.

CDSCO will thus be responsible for overall coordination and supervision of all pharmacovigilance activities under the Programme and performance of the various centres involved in this project.

**Incentives:**

It is hoped that the participating professionals can be provided motivation by allowing publication of pharmacovigilance data in medical journals and providing opportunities for continuous training for the professionals engaged in the Programme. There shall be provision for a contingency amount for each institution.

**Change of centre:**

Programme may move/shift if the centre coordinator is moving to another institution. Such a movement/shifting/transfer of a centre can only be done with the concurrence of the respective higher centre. The new institution to which the centre is proposed to be moved/shifted/transferred must also have relevant facilities for the Programme.

## 8. STEPS FOR FOSTERING “REPORTING CULTURE”

A periodic newsletter shall be published, may be quarterly, by the NPC, with the inputs and support from ZPCs. The publication may be printed or in an electronic format, and shall be widely circulated in the participating centres among doctors, nurses and pharmacists.

Professional bodies and non-government organizations [NGOs] shall be approached for collaboration.

Other promotional strategies that may be considered include:

- Posters
- Annual celebration of Pharmacovigilance Day
- Leaflets for patients / doctors
- Integrating pharmacovigilance learning sessions into undergraduate curriculum
- Interface with Indian Medical Association, Indian Pharmaceutical Association and other professional societies
- Email /referral system
- Cross links on the websites
- Pharmacovigilance-related articles in the newspapers/health journals
- A dedicated pharmacovigilance web site may be created by the NPC. While a dedicated web site is under preparation, a pharmacovigilance link may be provided from the CDSCO web site. The AE reporting form shall be available on the web site for health care professional to download or completion through a web based database.

## 9. WHAT TO REPORT

The National Pharmacovigilance Programme (NPP) shall encourage reporting of all **suspected** drug related adverse events, including those suspected to have been caused by herbal, traditional or alternative remedies. The reporting of seemingly insignificant or common adverse reactions would be important since it may highlight a widespread prescribing problem.

The programme particularly solicits reports of:

- ALL adverse events suspected to have been caused by new drugs and ‘Drugs of current interest’ (List to be published by CDSCO from time to time)
- ALL suspected drug interactions
- Reactions to **any** other drugs which are suspected of significantly affecting a patient’s management, including reactions suspected of causing:
  - death
  - life-threatening (real risk of dying)
  - hospitalisation (initial or prolonged)
  - disability (significant, persistent or permanent)
  - congenital anomaly
  - required intervention to prevent permanent impairment or damage

The prescribed ‘Adverse Drug Event Reporting Form’ shall be used for the purpose of National Pharmacovigilance Programme.

## **10. WHO CAN REPORT**

Any health care professionals (Doctors including Dentists, Nurses, and Pharmacists) may report suspected adverse drug events.

The Programme shall not accept reports from lay members of the public or anyone else who is not a health care professional.

## **11. WHERE TO REPORT**

After completion the form shall be returned/forwarded to the same Pharmacovigilance Centre from where it was received.

Reporting can be done to any one of the country wide Pharmacovigilance Centres nearest to the reporter. (complete list of Pharmacovigilance Centres is available at [www.cdsco.nic.in](http://www.cdsco.nic.in))

In case of doubt the form may be sent to the National Pharmacovigilance Centre at: Central Drugs Standard Control Organisation, Directorate General of Health Services, Ministry of Health & Family Welfare, Nirman Bhawan, New Delhi 110 011.

## **12. WHAT HAPPENS TO THE INFORMATION SUBMITTED**

The information in the form shall be handled in strict confidence. Peripheral Pharmacovigilance Centres shall forward the form to the respective Regional Pharmacovigilance Centres who will carry out the causality analysis. This information shall be forwarded to the Zonal Pharmacovigilance Centres. The data will be statistically analysed and forwarded to the global Pharmacovigilance Database managed by WHO Uppsala Monitoring Centre in Sweden.

The final report based on the analysed data will be periodically reviewed by the National Pharmacovigilance Advisory Committee constituted by the Ministry of Health and Family Welfare. The Committee is entrusted with the responsibility to review data and suggest any regulatory interventions that may be required with respect to the drug/drugs or class of drugs.

## **13. QUALITY OF SUSPECTED ADVERSE DRUG EVENT INFORMATION**

Only those forms which meet the following criteria shall be analysed:

- Authenticity (including reporter's and patient's traceability)
- Completeness (at least with respect to point no.'s 1, 5, 8, 11, 20 and 22 on the ADE Reporting Form)
- Legibility

In order to avoid receiving fake unauthentic reports or reports by parties having vested interests against any drug(s).it is important that the reporter's identity is clearly stated in the form so that the reporter can be approached to verify the authenticity of the entire report.

#### 14. CENTRE'S COORDINATORS' RESPONSIBILITIES AT DIFFERENT LEVELS OF PROGRAMME

Sl. No.	Responsibilities	PPC	RPC	ZPC
1.	To collect ADE notifications	√	√	√
2.	To receive blank ADE forms and acknowledge receipt	√	√	√
3.	To fill or get filled the ADE forms (fill all mandatory data)	√	√	√
4.	To forward duly-filled ADE forms to next higher level centre	√	√	
5.	To maintain a log of all ADE notification forms (blank or filled) received and forwarded	√	√	√
6.	To identify, induce PPC / RPC (with concurrence of NPC), provide them with general technical support, coordinate and monitor their functioning		√	√
7.	To identify and deploy a pharmacologist for management of pharmacovigilance tasks	√	√	
8.	To identify and deploy a data manager for data management under NPP			√
9.	To carry out (or review) causality analysis of all ADE forms or review such analysis by the RPC	Optional	√	√
10.	To forward all duly-filled ADE forms (those generated at the same centre and those received from immediate lower-level centre) as per pre-determined time line	* Weekly (Monday)	* Every 15 days (alternate Monday)	* Only archiving
11.	To report all serious adverse events within two week days, subsequent to receipt of its notification at the centre	√	√	√
12.	To forward periodic report to next higher centre as per the MIS format (appendix I)	Every 15 days (1st & 15th of every month)	Monthly (1st of every month)	Monthly (1st of every month)
13.	To liaison with healthcare professionals in order to inculcate / foster the culture of ADE notification / reporting 1. Acknowledge the cooperation by the notifier 2. Share with notifier relevant feedback from higher centres	√	√	√
14.	To organize and attend training programs / interactive meetings for all lower level centres	√	√	√

\*Information of all serious ADE's must be conveyed to the NPC within 2 working days by fax, email, telephone, courier as per stipulated guideline.

**Important:**

RPC and ZPC are acknowledged to have comparable professional competence. Their hierarchical position is only for administrative and management purposes (ZPC has the additional responsibilities for data collation, statistical analysis and archiving). Concurrence for selection of new PPCs / RPCs will be given by the ZPC in consultation with NPC. If a new centre is being proposed to replace a non functional PPC or RPC, the NPC and ZPC shall provide their opinion/concurrence in not more than one month.

New centres may join the Programme depending on the need in a particular territory and availability of resources to support new centre(s). The request may be forwarded through the respective RPC/ZPC to the NPAC which will take a final decision in this regard. In all cases, Head of the Institution desiring to join the Programme must give administrative clearance to this effect.

**16. MANAGEMENT INFORMATION SYSTEM REPORTS TO BE PROVIDED UNDER THE PROGRAMME**

<b>[PPC to RPC]</b>	<b>[RPC to ZPC]</b>	<b>[ZPC to NPC]</b>
<ol style="list-style-type: none"> <li>1. Period of the report</li> <li>2. No. of notifications received in the preceding period?</li> <li>3. No. of reports made</li> <li>4. No. of serious (or suspected serious) AE reports (if any)</li> <li>5. No. of serious (or suspected serious) AE reports forwarded within specified time</li> <li>6. No. of serious (or suspected serious) AE reports not forwarded within specified time</li> <li>7. Reasons for delay</li> <li>8. Important happenings or developments (events that happened other than the way they should have happened or events that dint happen the way they should have happened)</li> <li>9. Total No. of AE forms received</li> <li>10. No. of AE forms in which causality assessments made</li> <li>11. Any other observations</li> </ol>	<ol style="list-style-type: none"> <li>1. Period of the report</li> <li>2. No. of notifications received in the preceding period</li> <li>3. No. of reports made</li> <li>4. No. of serious (or suspected serious) AE reports (if any)</li> <li>5. No. of serious (or suspected serious) AE reports forwarded within specified time</li> <li>6. No. of serious (or suspected serious) AE reports not forwarded within specified time</li> <li>7. Reasons for delay</li> <li>8. Important happenings or developments (events that happened other than the way they should have happened or events that dint happen the way they should have happened)</li> <li>9. Total No. of AE forms received</li> <li>10. No. of AE forms in which causality assessments made</li> <li>11. New PPC identified and recommended if any</li> <li>12. No. of notifications/reports received from each centre</li> <li>13. No. of reports inappropriately filled in by respective PPCs</li> <li>14. Actions taken / recommended</li> <li>15. MONITORING activities done</li> <li>16. # / Acknowledgments sent in time</li> <li>17. CME awareness activities if any</li> <li>18. Any other observations</li> </ol>	<ol style="list-style-type: none"> <li>1. Period of the report</li> <li>2. No. of notifications received in the preceding period</li> <li>3. No. of reports made</li> <li>4. No. of serious (or suspected serious) AE reports (if any)</li> <li>5. No. of serious (or suspected serious) AE reports forwarded within specified time</li> <li>6. No. of serious (or suspected serious) AE reports not forwarded within specified time</li> <li>7. Reasons for delay</li> <li>8. Important happenings or developments (events that happened other than the way they should have happened or events that dint happen the way they should have happened)</li> <li>9. Total No. of AE forms received</li> <li>10. No. of AE forms in which causality assessments made</li> <li>11. No. of recommendations from RPC for new PPC</li> <li>12. No. of AE forms received from RPC in which causality assessment has been made</li> <li>13. No. of AE forms received from RPC in which causality assessment has been verified/reassessed (all SAEs and 10% of all remaining)</li> <li>14. No. of forms archived</li> <li>15. MONITORING activities done</li> </ol>

		16. No. of notifications/reports received from each centre 17. No. of reports filled in inappropriately by respective Regional Centres 18. Actions taken / recommended 19. # / Acknowledgments sent in time 20. CME & awareness activities if any 21. Any other observations
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### 17. PUBLICATION OF DATA

Centres may publish / make presentations based on the data generated by them but without directly or indirectly implying that the data has been generated and/or is a part of the NPP. Only NPAC may publish or authorise to publish any data or reports, with reference(s) made to the Programme.

No informed consent is needed to be obtained from patients' whose data is reported; Patients' identity is never revealed.

### 18. PERFORMANCE BENCHMARKS

Consequences of non-conformance with or violation of National Pharmacovigilance Protocol:

It will be the responsibility of the Coordinator of the respective higher Pharmacovigilance Centre to supervise and monitor the performance of the centres operating at the respective lower levels. In case of any non-conformance or violation of the Protocol, the supervising Coordinator shall issue (3 reminders at monthly intervals) to the concerned centre Coordinator a memorandum seeking conformance with the Protocol/Operating System. If no satisfactory response is received even after 3 reminders- the defaulting Centre shall be assumed to have withdrawn from the programme.

If an RPC gets closed down (or becomes non-operational due to any reasons), the ZPC will function in the interim as the RPC with immediate effect, until alternative arrangement is made. If a ZPC gets closed down (or becomes non-operational due to any reasons), the NPC will entrust any functional RPC the additional responsibility to function as a ZPC with immediate effect, until alternative arrangements are made.

Supervising/monitoring Pharmacovigilance Centre Coordinators should typically look for the following performance parameters:

- a. No. of reports per month
- b. Non compliance with protocol
- c. Violation of protocol
- d. Submission of fraudulent data and or other information
- e. Publication of data with mention of NPP, without appropriate authorisation from NPAC
- f. Any other professional/administrative misconduct concerning the NPP

## 19. RESOURCES FOR PHARMACOVIGILANCE CENTRES

The following books shall be provided to various centres as identified by the NPAC:

Current editions of:

- a. Meyler's Side Effects
- b. AHFS Drug Information hand book
- c. Martindale / online
- d. Davies Text Book of ADR
- e. Physician's Desk reference
- f. British National Formulary

Each ZPC will be provided funds to deploy a pharmacologist and a data manager. Each RPC will be provided funds to deploy a pharmacologist. Training programme shall be arranged for those healthcare professionals who are participating in NPP.

All centre coordinators will be provided training on the following issues:

- Skills to foster notification culture.
- Communications skills – for complete and meticulous collection of data.
- Methodology of filling up the forms

How often: At initiation of the programme / centres; subsequently every 6 months

Printed newsletter

For other medical colleges / centres / pharmacy colleges

Government bodies / NGOs

Medical associations

Regional and zonal centres are acknowledged to have comparable professional competence. Their hierarchical position is primarily for administrative and management purposes (zonal centres have the additional responsibilities for data collation and archiving). Concurrence/selection of Peripheral Centre /Regional Centres will be given by the zonal centre

Zonal centres to remain at the same venue even if the Coordinator moves to another institution.

If a new PPC wants to join the programme, its coordinator may write to the RC which will communicate to ZPC with a recommendation which then after concurrence informs the CDSCO

Programme may move/shift as recommended by Investigator who is moving with concurrence of next higher centre, provided the new location also has the facilities and the intent

– it will be assumed if no response in 30 days.

## **20. TERMS OF REFERENCE FOR ENGAGEMENT OF PERIPHERAL PHARMACOVIGILANCE CENTRE UNDER THE NATIONAL PHARMACOVIGILANCE PROGRAMME**

### **1. Background**

The Government of India with the assistance of World Bank has initiated the National Pharmacovigilance Programme. The Central Drugs Standard Control Organization (CDSCO) is coordinating the country-wide Pharmacovigilance programme under the aegis of DGHS, Ministry of Health & Family Welfare, New Delhi.

With the number of new drugs being regularly approved for marketing in India, there is a need for a vibrant Pharmacovigilance system in the country to protect our population from the potential harms that may be caused by some of these new drugs. Besides, with the patent regime coming in force from 2005, it is widely believed that India would become the global hub for new drug trials. These situations make it pertinent for the Indian central drugs regulatory authority to have a vibrant Pharmacovigilance system in the country.

The programme shall be coordinated by CDSCO under the supervision of a National Pharmacovigilance Advisory Committee which would monitor the program and also recommend regulatory interventions based on the generated Adverse Drug Reaction (ADR) data.

### **2. Objective of the Assignment**

Assignment: To manage the Peripheral Pharmacovigilance centre

The overall objective as per the National Pharmacovigilance Programme will be:

1. To monitor safety of the drugs and provide structured inputs for appropriate regulatory interventions
2. To create awareness about ADR monitoring in India

Peripheral centres will be the primary pharmacovigilance centres under the National Pharmacovigilance Programme.

To carry out the functions as envisaged in the "Protocol for the National Pharmacovigilance Programme" a Coordinator will have to be designated who will be in-charge of the pharmacovigilance activities at the designated peripheral centre.

By accepting to participate in the National Pharmacovigilance Programme all centres explicitly agree that all pharmacovigilance activities at their institutions shall be performed in strict consonance with the National Pharmacovigilance Programme appended here (Coordinators of the centres and heads of the institutions are advised to carefully go through the Protocol prior to joining the programme).

### 3. Outline of tasks to be carried out

The National Pharmacovigilance Programme encourages the reporting of all suspected adverse reaction to drugs and other medicinal substances including herbal, traditional or alternative remedies. The reporting of seemingly insignificant or common adverse reactions would be important since it may highlight a wide spread prescribing problem.

Peripheral Centre is expected to carry out the following tasks:

1. To maintain a log of all ADE notification forms received and forwarded
2. To receive blank ADE forms and acknowledge receipt
3. To fill or get filled the ADE forms
4. Collect & collate Adverse Drug notifications from own centres
5. Receive Adverse Drug Events (ADE) forms and maintain log of all ADE forms received and forwarded.
6. Correspond with Regional Centres for general technical support, and coordination
7. Carry out (and/or review) data causality analysis of all ADEs
8. To forward all duly-filled ADE forms [those generated at the same centre] as per pre-determined time line
9. Forward periodic reports to the CDSCO centre as per SI. No. 9
10. Liaise with health care professionals in order to inculcate / foster the culture of ADE reporting / notification by acknowledging the cooperation by the notifier and share with the notifier relevant feedback from higher centre.
11. Attend training programmes / interactive meetings for peripheral centres falling under the respective zonal pharmacovigilance centres
12. To provide updates, reports and such other information as may be required by the National Pharmacovigilance Advisory Committee and to attend their meetings
13. To conduct special pharmacovigilance projects on various drugs which may be of special concern or interest to CDSCO / Government of India
14. To maintain account of the funds provided under this program as per your institution's systems; To provide a consolidated statement to the regional centre
15. Carryout audits to ensure compliance with the program, enlist non-compliance, establish corrective measures and implement them at peripheral centres

In line with the size & patient intake of the institutions where it is based, the peripheral centre shall ensure a minimum 30 adverse event reportings every month and this number must be increased periodically. This number will be in addition to the number of reports generated by the zonal and regional centres falling under respective zonal centers.

#### 4. Schedule of Performance of Tasks

The duration of the assignment is four year (with a review at the end of every year). The time schedule for performance of various tasks is detailed below:

S. No.	Task	Time Schedule
1.	To maintain a log of all ADE notification forms received and forwarded	Ongoing
2.	To receive blank ADE forms and acknowledge receipt	Ongoing
3.	To fill or get filled the ADE forms	Ongoing
4.	Collect & collate Adverse Drug notifications from own centres	Monthly
5.	Receive Adverse Drug Events (ADE) forms and maintain log of all ADE forms received and forwarded.	Monthly.
6.	Carry out (and/or review) data causality analysis of all ADEs	Monthly
7.	To forward all duly-filled ADE forms as per pre-determined time line	Monthly
8.	Forward periodic reports to the CDSCO centre as per Sl. No. 9	1st and 15th of every month
9.	Liaise with health care professionals in order to inculcate / foster the culture of ADE reporting / notification by acknowledging the cooperation by the notifier and share with the notifier relevant feedback from higher centre.	Ongoing
10.	Organize and attend training programmes / interactive meetings	6 months in addition to induction training
11.	To provide updates, reports and such other information as may be required by the National Pharmacovigilance Advisory Committee and to attend their meetings	Ongoing
12.	To conduct special pharmacovigilance projects on various drugs which may be of special concern or interest to CDSCO / Government of India	Ongoing
13.	To maintain account of the funds provided under this program as per your institution's systems; To provide a consolidated statement to the national centre	Quarterly
14.	Carryout audits to ensure compliance with the program, enlist non-compliance, establish corrective measures and implement them	Quarterly

#### 5. Data Services and Facilities to be provided by CDSCO

CDSCO shall coordinate the programme and arrange for training for those professionals who are participating in the programme.

#### 6. Final Output that will be required

- a) Structured pharmacovigilance data based on the ADE forms collected under the program participants.
- b) A structured annual report describing smooth and efficient operation of the program, in accordance with the Protocol.

## **7. Financial support under the Project**

The following financial support shall be provided by CDSCO:

1. Expenditure on office operation for Zonal centre: Rs. 15,000.00 p.a.
2. AE Reporting forms, various books and periodicals, MIS reporting forms shall be provided by the CDSCO, which will also provide funds for zonal / regional / peripheral interaction meetings twice a year.

## **8. MIS Formats for Reporting by Proposal Centre to CDSCO**

1. Period of Report
2. Number of notifications received in the preceding period
3. Number of Reports made and number of serious or suspected serious AEs reports, if any
4. Number of serious or suspected serious AE reports forwarded with in the specified time
5. Number of serious or suspected serious AE reports not forwarded with in the specified time along with the reasons for delay
6. Important happenings or development (events that happened other than the way they should have happened or the events that did not happen other than the way they should have happened)
7. Total number of AEs forms received
8. Number of recommendations from Regional Pharmacovigilance centres for new peripheral pharmacovigilance centre
9. Number of forms archived
10. Monitoring activities done
11. No. of notifications / reports received from each centre
12. No. of reports filled in inappropriately by respective Peripheral Centre
13. Actions taken / recommended
14. Acknowledgements sent in time
15. CME awareness activities if any
16. Any other observations

## **21. Terms of Reference for engagement of Regional Pharmacovigilance Centre under the National Pharmacovigilance Programme**

### **1. Background**

The Government of India with the assistance of World Bank has initiated the National Pharmacovigilance Programme. The Central Drugs Standard Control Organization (CDSCO) is coordinating the country-wide Pharmacovigilance programme under the aegis of DGHS, Ministry of Health & Family Welfare, New Delhi.

With the number of new drugs being regularly approved for marketing in India, there is a need for a vibrant Pharmacovigilance system in the country to protect our population from the potential harms that may be caused by some of these new drugs. Besides, with the patent regime coming in force from 2005, it is widely believed that India would become the global hub for new drug trials. These situations make it pertinent for the Indian central drugs regulatory authority to have a vibrant Pharmacovigilance system in the country.

The programme shall be coordinated by CDSCO under the supervision of a National Pharmacovigilance Advisory Committee which would monitor the program and also recommend regulatory interventions based on the generated Adverse Drug Reaction (ADR) data.

### **2. Objective of the Assignment**

Assignment: To manage the Regional Pharmacovigilance centre (covering \* regions)

The overall objective as per the National Pharmacovigilance Programme will be:

3. To monitor safety of the drugs and provide structured inputs for appropriate regulatory interventions
4. To create awareness about ADR monitoring in India

Regional centres will be the secondary pharmacovigilance centres under the National Pharmacovigilance Programme.

To carry out the functions as envisaged in the "Protocol for the National Pharmacovigilance Programme" a Coordinator will have to be designated who will be in-charge of the pharmacovigilance activities at the designated regional centre.

By accepting to participate in the National Pharmacovigilance Programme all centres explicitly agree that all pharmacovigilance activities at their institutions shall be performed in strict consonance with the National Pharmacovigilance Programme appended here (Coordinators of the centres and heads of the institutions are advised to carefully go through the Protocol prior to joining the programme).

### **3. Outline of tasks to be carried out**

The National Pharmacovigilance Programme encourages the reporting of all suspected adverse reaction to drugs and other medicinal substances including herbal, traditional or alternative remedies. The reporting of seemingly insignificant or common adverse reactions would be important since it may highlight a wide spread prescribing problem.

Regional Centre is expected to carry out the following tasks:

1. To maintain a log of all ADE notification forms received and forwarded
2. To receive blank ADE forms and acknowledge receipt
3. To fill or get filled the ADE forms
4. Collect & collate Adverse Drug notifications from Peripheral as well as own centres
5. Receive Adverse Drug Events (ADE) forms and maintain log of all ADE forms received and forwarded.
6. Correspond with Peripheral Centres, provide them with general technical support, coordinate and monitor their functioning.
7. Identify and delegate a pharmacologist for management of pharmacovigilance tasks.
8. Carry out (and/or review) data causality analysis of all ADEs
9. To forward all duly-filled ADE forms [those generated at the same centre and those received from immediate lower-level centre] as per pre-determined time line
10. Forward periodic reports to the CDSCO centre as per Sl. No. 9
11. Liaise with health care professionals in order to inculcate / foster the culture of ADE reporting / notification by acknowledging the cooperation by the notifier and share with the notifier relevant feedback from higher centre.
12. Organize and attend training programmes / interactive meetings for all peripheral centres falling under the respective regional pharmacovigilance centres
13. To provide updates, reports and such other information as may be required by the National Pharmacovigilance Advisory Committee and to attend their meetings
14. To conduct special pharmacovigilance projects on various drugs which may be of special concern or interest to CDSCO / Government of India
15. To maintain account of the funds provided under this program as per your institution's systems; To review the account statement received from peripheral centres, and provide a consolidated statement to the zonal centre
16. Carryout audits to ensure compliance with the program, enlist non-compliance, establish corrective measures and implement them at regional centres and oversee their implications at peripheral centres

In line with the size & patient intake of the institutions where it is based, the regional centre shall ensure a minimum 50 adverse event reportings every month and this number must be increased periodically. This number will be in addition to the number of reports generated by the peripheral centres falling under respective regional centers.

#### 4. Schedule of Performance of Tasks

The duration of the assignment is four year (with a review at the end of every year). The time schedule for performance of various tasks is detailed below:

S. No.	Task	Time Schedule
1.	To maintain a log of all ADE notification forms received and forwarded	Ongoing
2.	To receive blank ADE forms and acknowledge receipt	Ongoing
3.	To fill or get filled the ADE forms	Ongoing
4.	Collect & collate Adverse Drug notifications from Peripheral as well as own centres	Monthly
5.	Receive Adverse Drug Events (ADE) forms and maintain log of all ADE forms received and forwarded.	Monthly.
6.	Correspond with Peripheral Centres, provide them with general technical support, coordinate and monitor their functioning.	One month from the date of appointment
7.	Identify and delegate a pharmacologist for management of pharmacovigilance tasks.	One month from date of appointment
8.	Identify and delegate a data manager for the data management under National Pharmacovigilance Programme	
9.	Carry out (and/or review) data causality analysis of all ADEs	Monthly
10.	To forward all duly-filled ADE forms [those generated at the same centre and those received from immediate lower-level centre] as per pre-determined time line	Monthly
11.	Forward periodic reports to the CDSCO centre as per Sl. No. 9	1st and 15th of every month
12.	Liaise with health care professionals in order to inculcate / foster the culture of ADE reporting / notification by acknowledging the cooperation by the notifier and share with the notifier relevant feedback from higher centre.	Ongoing
13.	Organize and attend training programmes / interactive meetings for all peripheral centres falling under the respective regional pharmacovigilance centres	6 months in addition to induction training
14.	To provide updates, reports and such other information as may be required by the National Pharmacovigilance Advisory Committee and to attend their meetings	Ongoing
15.	To conduct special pharmacovigilance projects on various drugs which may be of special concern or interest to CDSCO / Government of India	Ongoing
16.	To maintain account of the funds provided under this program as per your institution's systems; To review the account statement received from peripheral centres, and provide a consolidated statement to the zonal centre	Quarterly
17.	Carryout audits to ensure compliance with the program, enlist non-compliance, establish corrective measures and implement them at regional centres and oversee their implications at peripheral centres	Quarterly

5. **Data Services and Facilities to be provided by CDSCO**  
CDSCO shall coordinate the programme and arrange for training for those professionals who are participating in the programme.
6. **Final Output that will be required**
  - c) Structured pharmacovigilance data based on the ADE forms collected under the program participants.
  - d) A structured annual report describing smooth and efficient operation of the program, in accordance with the Protocol.
7. **Financial support under the Project**  
The following financial support shall be provided by CDSCO:
  1. One post of Pharmacologist: Minimum qualification: M.Pharm., Desired Qualification: M.Pharm. with pharmacology or clinical pharmacy. Maximum remuneration of Rs. 15,000.00 (fixed)
  2. All staff members shall be identified and retained by the regional centres on contract on year to year basis
  3. Expenditure on office operation for regional centre: Rs. 25,000.00 p.a.
  4. AE Reporting forms, various books and periodicals, MIS reporting forms shall be provided by the CDSCO, which will also provide funds for zonal / regional / peripheral interaction meetings twice a year.
8. **MIS Formats for Reporting by Regional Centre to Zonal Centre**
  1. Period of Report
  2. Number of notifications received in the preceding period
  3. Number of Reports made and number of serious or suspected serious AEs reports, if any
  4. Number of serious or suspected serious AE reports forwarded with in the specified time
  5. Number of serious or suspected serious AE reports not forwarded with in the specified time along with the reasons for delay
  6. Important happenings or development (events that happened other than the way they should have happened or the events that did not happen other than the way they should have happened)
  7. Total number of AEs forms received
  8. Number of recommendations from Peripheral Pharmacovigilance centres for new peripheral pharmacovigilance centre
  9. Total no. of AE forms received from Peripheral Centre in which causality assessments has been made
  10. Number of AE forms received from Peripheral Centre in which causality assessment has been verified / reassessed
  11. Number of forms archived
  12. Monitoring activities done
  13. No. of notifications / reports received from each centre
  14. No. of reports filled in inappropriately by respective Peripheral Centres
  15. Actions taken / recommended
  16. Acknowledgements sent in time
  17. CME awareness activities if any
  18. Any other observations

## **22. Terms of Reference for engagement of Zonal Pharmacovigilance Centre under the National Pharmacovigilance Programme**

### **1. Background**

The Government of India with the assistance of World Bank has initiated the National Pharmacovigilance Programme. The Central Drugs Standard Control Organization (CDSCO) is coordinating the country-wide Pharmacovigilance programme under the aegis of DGHS, Ministry of Health & Family Welfare, New Delhi.

With the number of new drugs being regularly approved for marketing in India, there is a need for a vibrant Pharmacovigilance system in the country to protect our population from the potential harms that may be caused by some of these new drugs. Besides, with the patent regime coming in force from 2005, it is widely believed that India would become the global hub for new drug trials. These situations make it pertinent for the Indian central drugs regulatory authority to have a vibrant Pharmacovigilance system in the country.

The programme shall be coordinated by CDSCO under the supervision of a National Pharmacovigilance Advisory Committee which would monitor the program and also recommend regulatory interventions based on the generated Adverse Drug Reaction (ADR) data.

### **2. Objective of the Assignment**

Assignment: To manage the Zonal Pharmacovigilance centre (covering \* regions)

The overall objective as per the National Pharmacovigilance Programme will be:

5. To monitor safety of the drugs and provide structured inputs for appropriate regulatory interventions
6. To create awareness about ADR monitoring in India

Zonal centres will be the tertiary pharmacovigilance centres under the National Pharmacovigilance Programme.

To carry out the functions as envisaged in the "Protocol for the National Pharmacovigilance Programme" a Coordinator will have to be designated who will be in-charge of the pharmacovigilance activities at the designated zonal centre.

By accepting to participate in the National Pharmacovigilance Programme all centres explicitly agree that all pharmacovigilance activities at their institutions shall be performed in strict consonance with the National Pharmacovigilance Programme appended here (Coordinators of the centres and heads of the institutions are advised to carefully go through the Protocol prior to joining the programme).

### 3. Outline of tasks to be carried out

The National Pharmacovigilance Programme encourages the reporting of all suspected adverse reaction to drugs and other medicinal substances including herbal, traditional or alternative remedies. The reporting of seemingly insignificant or common adverse reactions would be important since it may highlight a wide spread prescribing problem.

Zonal Centre is expected to carry out the following tasks:

1. To maintain a log of all ADE notification forms received and forwarded
2. To receive blank ADE forms and acknowledge receipt
3. To fill or get filled the ADE forms
4. Collect & collate Adverse Drug notifications from Regional as well as own centres
5. Receive Adverse Drug Events (ADE) forms and maintain log of all ADE forms received and forwarded.
6. Correspond with Regional Centres, provide them with general technical support, coordinate and monitor their functioning.
7. Identify and delegate a pharmacologist for management of pharmacovigilance tasks.
8. Identify and delegate a data manager for the data management under National Pharmacovigilance Programme
9. Carry out (and/or review) data causality analysis of all ADEs
10. To forward all duly-filled ADE forms [those generated at the same centre and those received from immediate lower-level centre] as per pre-determined time line
11. Forward periodic reports to the CDSCO centre as per Sl. No. 9
12. Liaise with health care professionals in order to inculcate / foster the culture of ADE reporting / notification by acknowledging the cooperation by the notifier and share with the notifier relevant feedback from higher centre.
13. Organize and attend training programmes / interactive meetings for all regional and peripheral centres falling under the respective zonal pharmacovigilance centres
14. To provide updates, reports and such other information as may be required by the National Pharmacovigilance Advisory Committee and to attend their meetings
15. To conduct special pharmacovigilance projects on various drugs which may be of special concern or interest to CDSCO / Government of India
16. To maintain account of the funds provided under this program as per your institution's systems; To review the account statement received from regional centres, and provide a consolidated statement to the national centre
17. Carryout audits to ensure compliance with the program, enlist non-compliance, establish corrective measures and implement them at zonal centres and oversee their implications at regional centres

In line with the size & patient intake of the institutions where it is based, the zonal centre shall ensure a minimum 100 adverse event reportings every month and this number must be increased periodically. This number will be in addition to the number of reports generated by the regional and peripheral centres falling under respective zonal centers.

#### 4. Schedule of Performance of Tasks

The duration of the assignment is four year (with a review at the end of every year). The time schedule for performance of various tasks is detailed below:

S. No.	Task	Time Schedule
1.	To maintain a log of all ADE notification forms received and forwarded	Ongoing
2.	To receive blank ADE forms and acknowledge receipt	Ongoing
3.	To fill or get filled the ADE forms	Ongoing
4.	Collect & collate Adverse Drug notifications from Regional as well as own centres	Monthly
5.	Receive Adverse Drug Events (ADE) forms and maintain log of all ADE forms received and forwarded.	Monthly.
6.	Correspond with Regional Centres, provide hem with general technical support, coordinate and monitor their functioning.	One month from the date of appointment
7.	Identify and delegate a pharmacologist for management of pharmacovigilance tasks.	One month from date of appointment
8.	Identify and delegate a data manager for the data management under National Pharmacovigilance Programme	
9.	Carry out (and/or review) data causality analysis of all ADEs	Monthly
10.	To forward all duly-filled ADE forms [those generated at the same centre and those received from immediate lower-level centre] as per pre-determined time line	Monthly
11.	Forward periodic reports to the CDSCO centre as per Sl. No. 9	1st and 15th of every month
12.	Liaise with health care professionals in order to inculcate / foster the culture of ADE reporting / notification by acknowledging the cooperation by the notifier and share with the notifier relevant feedback from higher centre.	Ongoing
13.	Organize and attend training programmes / interactive meetings for all regional and peripheral centres falling under the respective zonal pharmacovigilance centres	6 months in addition to induction training
14.	To provide updates, reports and such other information as may be required by the National Pharmacovigilance Advisory Committee and to attend their meetings	Ongoing
15.	To conduct special pharmacovigilance projects on various drugs which may be of special concern or interest to CDSCO / Government of India	Ongoing
16.	To maintain account of the funds provided under this program as per your institution's systems; To review the account statement received from regional centres, and provide a consolidated statement to the national centre	Quarterly
17.	Carryout audits to ensure compliance with the program, enlist non-compliance, establish corrective measures and implement them at zonal centres and oversee their implications at regional centres	Quarterly

## **5. Data Services and Facilities to be provided by CDSCO**

CDSCO shall coordinate the programme and arrange for training for those professionals who are participating in the programme.

## **6. Final Output that will be required**

- e) Structured pharmacovigilance data based on the ADE forms collected under the program participants.
- f) A structured annual report describing smooth and efficient operation of the program, in accordance with the Protocol.

## **7. Financial support under the Project**

The following financial support shall be provided by CDSCO:

- 1. One post of Pharmacologist: Minimum qualification: M.Pharm., Desired Qualification: M.Pharm. with pharmacology or clinical pharmacy. Maximum remuneration of Rs. 15,000.00 (fixed)
- 2. Computer Operator / Data Manager: With suitable qualification and/or experience. Maximum remuneration of Rs. 8,500.00 (fixed)

All staff members shall be identified and retained by the zonal centres on contract on year to year basis

- 3. Expenditure on office operation for Zonal centre: Rs. 25,000.00 p.a.
- 4. AE Reporting forms, various books and periodicals, MIS reporting forms shall be provided by the CDSCO, which will also provide funds for zonal / regional / peripheral interaction meetings twice a year.

## **8. MIS Formats for Reporting by Zonal Centre to CDSCO**

- 1. Period of Report
- 2. Number of notifications received in the preceding period
- 3. Number of Reports made and number of serious or suspected serious AEs reports, if any
- 4. Number of serious or suspected serious AE reports forwarded with in the specified time
- 5. Number of serious or suspected serious AE reports not forwarded with in the specified time along with the reasons for delay
- 6. Important happenings or development (events that happened other than the way they should have happened or the events that did not happen other than the way they should have happened)
- 7. Total number of AEs forms received
- 8. Number of recommendations from Regional Pharmacovigilance centres for new peripheral pharmacovigilance centre
- 9. Total no. of AE forms received from Regional Centre in which causality assessments has been made
- 10. Number of AE forms received from Regional Centre in which causality assessment has been verified / reassessed
- 11. Number of forms archived
- 12. Monitoring activities done

13. No. of notifications / reports received from each centre
14. No. of reports filled in inappropriately by respective Regional Centres
15. Actions taken / recommended
16. Acknowledgements sent in time
17. CME awareness activities if any
18. Any other observations