IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

PHARMACOVIGILANCE: AN OVERVIEW

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ABSTRACT:

Pharmacovigilance is defined by WHO as the science and activities relating to the detection, assessment, understanding and prevention of the adverse effects of drugs or any other possible drug-related problems. Adverse drug reactions (ADRs) are ranked as the top 10 leading causes of mortality and morbidity in the world. Pharmacovigilance is concerned about evaluating and monitoring the safety of medicine in clinical practice to improve patient's safety. Pharmacovigilance promotes safety and efficacy of the drug. The preliminary essential steps of pharmacovigilance is the reporting of suspected adverse drug events. PV evidence of medicine related problems like poor quality drugs, treatment failure, drug interaction. The Pharmacovigilance exertion in India is organized by The Indian Pharmacopoeia Commission and conducted by the Central Drugs Standard Control Organization (CDSCO). The fundamental aim of PvPI is to collect data, method, analyze it and provide necessary interventions to Health care professionals to minimizing the potential risks associated with the drug or blood and blood products. Pharmacists contribute to the drug safety by preventing, identifying, documenting, and reporting of ADRs.

KEYWORDS: Pharamacovigilance, adverse effects, importance, PvPI.

INTRODUCTION:[1-8]

Pharmacovigilance (PV) was officially introduced in December 1961 with the publication of a letter (case report) in the Lancet by W. McBride, the Australian doctor who first suspected a causal link between serious fetal deformities (phocomelia) and thalidomide, a drug used during pregnancy: Thalidomide was used as an antiemetic and sedative agent in pregnant women. In 1968, the World Health Organization (WHO) promoted the “Programme for International Drug Monitoring”, a pilot project aimed to centralize world data on adverse drug reactions (ADRs). In particular, the main aim of the “WHO Programme” was to identify the earliest possible PV signals. The term PV was proposed in the mid-70s by a French group of pharmacologists and toxicologists

to define the activities promoting "The assessment of the risks of side effects potentially associated with drug treatment". preventing harm to patients. The challenge of maximizing drug safety and maintaining public confidence has become increasingly complex. Pharmaceutical and biotechnology companies must not only monitor, but also proactively estimate and manage drug risk throughout a product's lifecycle, from development to post-market.

PV is particularly concerned with ADRs, which are drug responses that are noxious and unintended, and which occur at doses normally used for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function. Continuous monitoring of drug effects, side effects, contraindications and outright harmful effects which could result in a high degree of morbidity, and in some cases, even mortality, are essential to maximize benefits and minimize risks. No degree of care and caution at the pre-clinical and clinical testing stages can guarantee absolute safety, when a drug is marketed and prescribed to large populations across the country and outside. Because clinical trials involve several thousands of patients at most, less common side effects and ADRs are often unknown at the time a drug enters the market. Post marketing PV uses tools such as data mining and investigation of case reports to identify the relationships between drugs and ADRs. The drug regulatory agencies have the responsibility of having a well-established PV system to monitor ADRs during the drug development phase and later during the life time of a marketed drug.

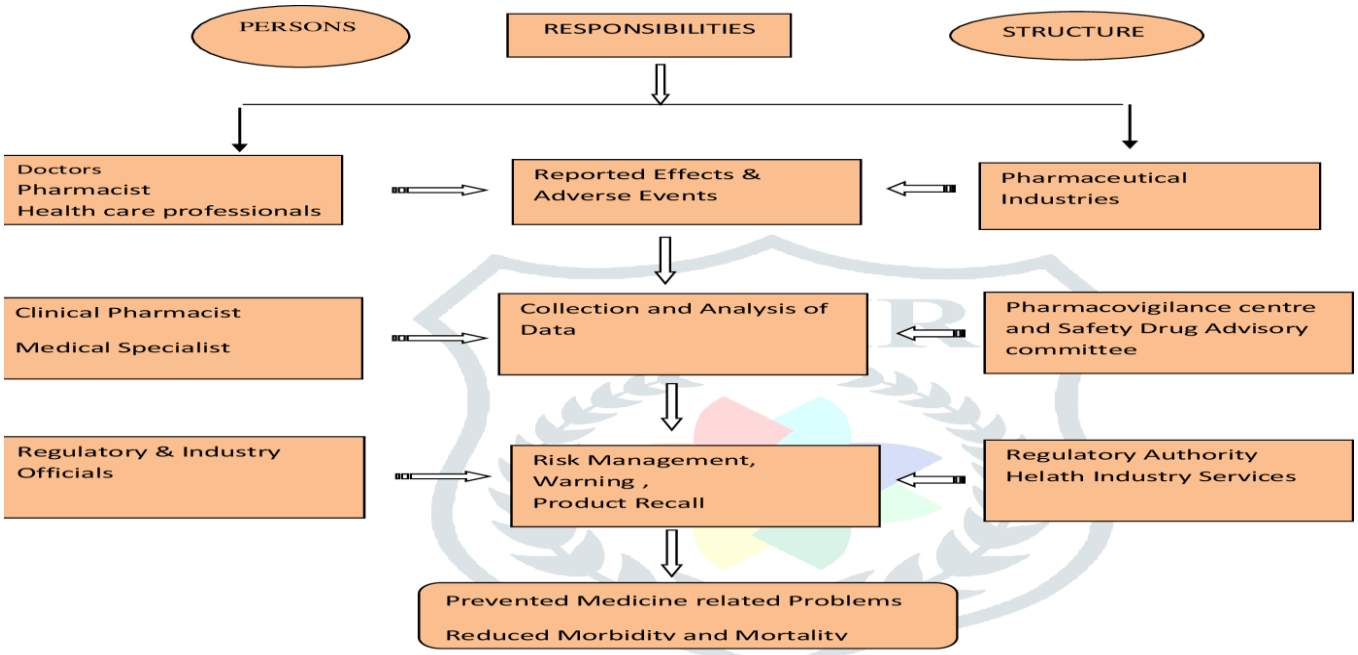
A complex and vital relationship exists between wide ranges of partners in the practice of drug safety monitoring such as government, industry, health care centers, hospitals, academia, medical and pharmaceutical associations, poisons information centers, health professionals, patients, consumers and media. Sustained collaboration and commitment are vital if future challenges in PV are to be met in order to develop and flourish. Since very few new drugs were discovered in India and hardly any new drug was launched for the first time in India in the past, there was no major compulsion to have a strong PV system to detect ADRs of marketed products. The experience from the markets where the drug was in use for several years before its introduction in India, was used by the companies and the regulatory agencies to assess the safety parameters and take corrective actions, such as the withdrawal or banning of the drug in question. The evolution of a new patent regime in the Indian pharmaceutical and biotechnology industries as a Trade Related Intellectual Property Rights and Services (TRIPS) makes it incumbent upon India to no longer copy patented products and marketthem without license from the innovator company. The leading Indian companies, realizing the compulsions of the new regime, have already initiated investments of substantial resources for the discovery and development of new drugs needed for both Indian and International markets. This in turn means that during the coming year, research and development by the Indian pharmaceutical and biotech companies will hopefully lead to new drugs based on pre-clinical and clinical data generated mostly in India. In such cases, the Indian regulatory agencies cannot count on the experience of other markets to assess the incidence and prevalence of importance of a properly designed PV system in India. With the Indian companies' capacity to develop and market new drugs out of their own research efforts, it is important that adequate PV standards are introduced to monitor ADRs of products first launched in India.

HISTORICAL BACKGROUND OF PV:[9-14]

The safety of drug was not the early concern in the history of drug. The thalidomide tragedy of 1960‟s opened the eyes of drug regulators as well as other concern healthcare professionals to establish a way to ensure drug safety. The mile stone in the drug safety was the publication of chloroform related death on The Lancet journal for the first time in 1893.Onwards, safety of drug became the global concern and different initiatives were taken by different country to safeguard the public health safety. The US Federal, Food and Drug (US FDA) act was passed in 1906 for the first time, but it was amended to control misbranding of ingredients and false advertising clams after the deaths associated with sulphanilamide elixir.There were 107 deaths by the use of diethylene glycol as a solvent for sulphanilamide elixir. There were radical changes in the drug safety issues after the worldwide thalidomide tragedy which was first reported by an Australian obstetrician, William McBride in 1961.He reported thalidomide associated “seal limbs” in the baby, used in pregnancy. This drug had not been adequately screened for teratogenic effects, but similar malformations were subsequently shown in the rabbit and (at high dose) in the rat. In West Germany 4000 individuals were affected. The tragedy made the world to be more concern about the drug safety, as efficacy was only the parameter to see the effect of drugs. Immediately after the tragedy the US FDA act was amended to compulsory premarketing submission of both efficacy and safety data in 1962. The UK Medicines act was enforced in 1968, however, safety monitoring via “yellow card system” was introduced in 1964. The drug safety issues were lobalised, strengthen and systematized after the establishment of World Health Organization (WHO) Programme for International Drug Monitoring in 1968. The Uppsala Monitoring Centre (UMC) located at Uppsala, Sweden co-ordinates the International Drug Monitoring program. Till now there are 104 official member countries and 33 associate members throughout the world, including developed, developing and under-developed country.

SCOPE OF PV:[15]

The discipline of PV has developed considerably since the 1972 WHO technical report, and it remains a dynamic clinical and scientific discipline. It has been essential to meet the challenges of the increasing range and potency of pharmaceutical and biological medicines including vaccines, which carry with them an inevitable and sometimes unpredictable potential for harm. The risk of harm, however, is less when medicines are used by an informed health profession and by patients who themselves understand and share responsibility for their drugs. When adverse effects and toxicity appear, particularly when previously unknown in association with the medicine, it is essential that they are analyzed and communicated effectively to an audience that has the knowledge to interpret the information. This is the role of PV, of which much has already been achieved. But more is required for the integration of the discipline into clinical practice and public policy. To fulfill the PV obligations for its marketed products as per regulations, a pharmaceutical company in India has to essentially carry out activities such as collection, and expedited reporting of serious unexpected ADRs.A typical setup for PV studies, including people involved on various levels, organizational units and their functions.



AIMS OF PHARMACOVIGILANCE:[16]

Thalidomide tradedy evidence the importance of effective drug monitoring system. The main aim of pharmacovigilance includes:

♣ Improvement of patient care and safety in relation to the use of medicine thereby enhance public health and safety.

♣ It asses the benefit, harm, effectiveness and risk of medicines that propagates the needful information to facilitate proper drug prescription and regulation.

♣ It provides the effective communication to health professionals and the public by strengthen the education, knowledge and clinical trials in pharmacovigilance.

♣ Early detection of unknown ADR and interaction and also identify the increase in the frequency of know adverse effects and their risk factors.

IMPORTANCE OF PHARMACOVIGILANCE:[17-29]

The Pharmacovigilance ensures patient safety throughout the development of drug and also after the drug reaches the market. It is used to identify the adverse effects of drug that enables the wellbeing of public. It provides evidence of medicine related problems like poor quality drugs, treatment failure, drug interaction. Promote safety to vulnerable groups such as Pregnant women & breastfeeding mother, elderly, young children.

Drug Regulation

A new medicine must pass three hurdles before its approval by the national drug regulatory authority. Sufficient evidence is required to show the new drug to be

• Of good quality,

• Effective, and

• Safe for the purpose or purposes for which it is proposed.

A. Clinical Trial Regulation

For drug regulators, the changing trends over recent years in the conduct of clinical trials present special and urgent challenges, particularly in ensuring that the rights and health of patients and their communities are protected. As the increasing complexity of clinical trialspresents further challenges to regulators that results in increased number of study designs.Local ethics committees and drug regulators are not always aware of patients and investigators experiences. This may affects the safety of patients and therefore Safety monitoring during clinical trials is considered as one of the major concerns for new drug development. This is currently being addressed by a CIOMS working group and it results in:

1) The collection of adverse experience information

2) Assessment/monitoring of clinical data

3) Reporting/communication of clinical data

B. Post-marketing safety monitoring

The stronger the national system of pharmacovigilance and ADR reporting, the more likely it is that reasonable regulatory decisions will be made for the early release of new drugs with the promise of therapeutic advances. It plays an important role in the introduction of generic medicines, and in review of the safety profile of older medicines already available, where new safety issues may have arisen. Post marketing safety monitoring stimulate the • Detection of drug interactions • measuring the environmental burden of medicines used in large populations • assessing the contribution of „inactive‟ ingredients (excipients) to the safety profile • systems for comparing safety profiles of similar medicines • surveillance of the adverse effects on human health of drug residues in animals, e.g. antibiotics and hormones.

C. Promotional activities

Promotional activity issues suggest the requirement for more thorough monitoring of drug safety and scrutiny of advertising. Resources and expertise are necessary to ensure that promotional materials contain accurate and balanced information, and that practices are ethical. The involvement of regional or international collaboration in the implementation of a regulatory code of practice for advertizing medicinal products would help the situation.

D. Pharmacovigilance and the national drug regulatory authority

The ultimate aim of National drug regulatory authority is to ensure the quality, safety and efficacy of all marketed products across the country. It includes:

• Promoting medicine safety by collecting and managing reports of ADRs, medication errors, and suspected substandard products.

- Collaborating and harmonizing with existing ADE reporting and collection activities within the country (e.g., national disease control programs, Ministry of Health) as well as international cohorts monitoring ADEs in defined patients or populations.

- Identifying safety signal (e.g., unknown or poorly characterized adverse events) in relation to a medicine or a combination of medicines.

- Undertaking a risk assessment and developing options for risk management.

- Identifying quality problems with medicines resulting in ADEs and supporting the identification of medicine quality issues in general.

- Providing effective communication on aspects of medicine safety, including prompt notification of confirmed safety and quality problems and dispelling unfounded rumors of toxicity attributed to medicines and vaccines.

- Applying PV information for the benefit of public health programs, individual patients, and national medicine policies and treatment guidelines.

- Developing and maintaining drug utilization information

- Identifying issues associated with inappropriate prescribing and dispensing of medicines1

E. Promoting communication in the field of drug safety

For the communication of adverse reactions or any other safety finding to regulators, health professionals and patient. Pharmacovigilance providesignificant ability and resources to evaluate and make suggestion on drug safety and efficacy. The major challenges for National centers, is to promote and maintain effective and open communication of information regarding the benefit, harm, effectiveness and risk of medicines, including the uncertainty of knowledge in this area, with the public and the health professions. The 1998 Erice Declaration on Communicating Drug Safety Information called for a united effort on the part of all interested parties in establishing a new culture of transparency, equity and accountability in the communication of drug safety information.

F. Risk and crisis management

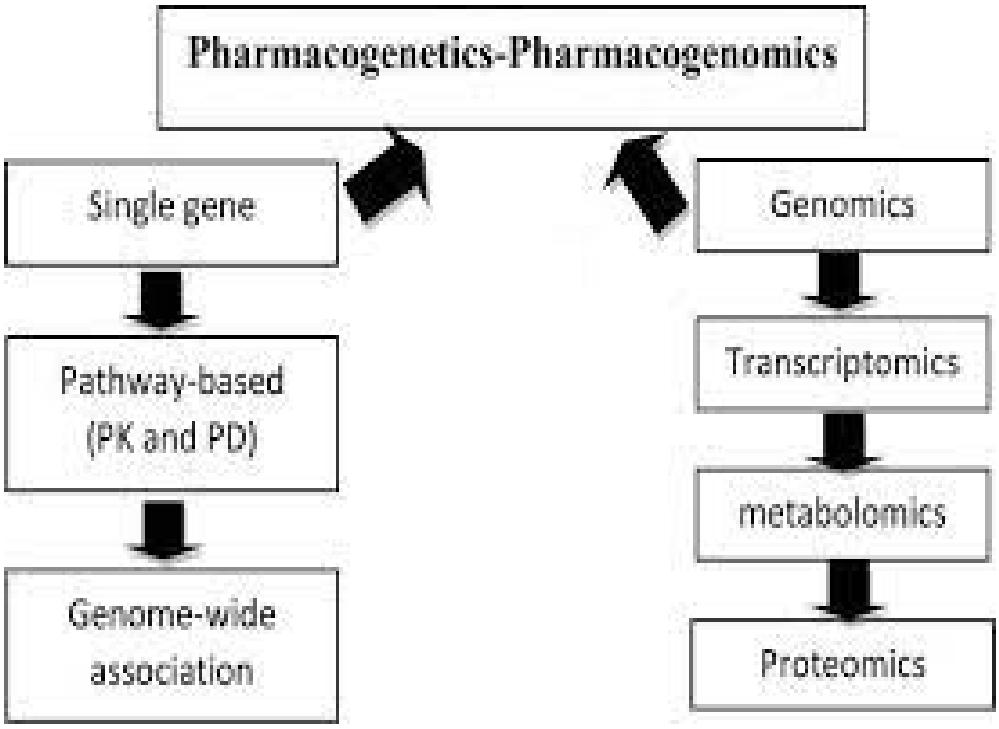
World Health Organization (WHO) defines a crisis as any unplanned event or succession of events which lead to interruption or destabilization of the normal operations or activities of an organization.Prevention of occurring drug safety problems is an essential section of drug safety crises management. This could be useful for reducing drug related morbidity and mortality.Risk Management Plans(RMP) and Risk Evaluation and Mitigation Strategies(REMS) are now a standard part of pharmacovigilance planning. The aim of both the RMP and the REMS is to reduce the risks related to a medicinal product through interventions and to disseminate those risks to patients and healthcare providers. Medication guides, a detailed communication plan about safety issues, specific elements to assure safe use of a product such as required laboratory testing or prescriber training, an implementation plan and a timetable for assessment.

G. Herbal and Traditional Medicines

Misuse of the wrong species of medicinal plants, inappropriate dosing, errors in the use of herbal medicines by healthcare providers and consumers, interactions with other medicines results in Adverse effects. The purpose of pharmacovigilance is to detect, assess, and understand, and to prevent the adverse effects or any other possible drug-related problems, related to herbal, traditional, and complementary medicines. In order to provide consistency in the naming of herbs in adverse reaction (AR) reports, the WHO Collaborating Centre for International Drug Monitoring has recommended the use of proper scientific binomial names for herbs used in medicine, including the use of such names (where this information is available) in the coding of AR reports. This will assure the comparability between reports from various international pharmacovigilance databases. To handle herbal medicines and, in particular, to analyze the causes of adverse events, the national pharmacovigilance centers (or equivalent institutions) will include trained personnel in the relevant technical areas and facilities to analyze the products concerned, for which there is often insufficient information and lack of access to reliable information support.

ROLEOFPHARMACOGENOMICSIN PV:[30-31]

Pharmacogenomics (PGx) combines traditional pharmaceutical sciences such as biochemistry with annotated knowledge of genes, proteins, and single nucleotide polymorphisms (SNP). It is the technology that deals with the influence of genetic variation on drug response in patients by correlating gene expression or single-nucleotide polymorphisms (SNP) with a drug's efficacy or toxicity. By doing so, (PGx) aims to develop rational means to optimize drug therapy, with respect to the patients' genotype, to ensure maximum efficacy with minimal adverse effects.Such approaches promise the advent of "personalized medicine"; in which drugs and drug combinations are optimized for each individual's unique genetic makeup. The science of Role of Pharmacovigilance in India: An Overview 9 Online Journal of Public Health Informatics pharmacogenetics (PG) originated from the analysis of a few rare and sometimes serendipitously found extreme reactions (phenotypes) observed in some humans. These phenotypes were either inherited diseases or abnormal reactions to drugs or other environmental factors. PG and PGx research remain iterative processes and there is more room for opportunities for improvement in each of the approaches. Figure 3 shows that multiple approaches have to be combined to obtain PGx knowledge that is of value for the development of new therapeutics or for the improvement of existing therapies.



PHARMACOVIGILANCE AND DRUG SAFETY MONITORING:[32-36]

Every drug is associated with beneficial as well as undesirable or adverse effect. ADR as defined by WHO is "noxious or unintended response to a drug occurs at a usual dose". ADR is broadly classified as Type A and Type B. Type A reaction is associated with the pharmacological actions of the drug and is predictable while Type B reaction is not associated with the pharmacological actions of the drug and is not predictable. It is also known as idiosyncratic reaction. Type A reaction is more prevalent, accounts for more than 80%, than the Type B reaction. ADRs are associated with significant morbidity and mortality. Recent estimates suggest ADRs are the fourth to sixth major cause of death in the United States of America (USA). The hospitalization due to ADRs in some countries is about or more than 10%, which means ADRs as a major cause of hospitalization. In addition, it is estimates that 10-20% of the hospital inpatient suffers from ADRs. That's why ADRs is the common clinical problem. Appropriate monitoring of ADRs is the only best way to safeguard the patients and even prevents ADRs.

The term pharmacovigilance is a French world, which has been described by Professor Bernard Begaud as "a discipline involving detection, evaluation and prevention of undesirable effects of medicines". Another definition as described by Professor Lawson is as "part of the science of pharmacoepidemiology". The WHO defines pharmacovigilance as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems".

SIGNAL AND METHODOLOGY IN PHARMACOVIGILANCE: [37-40]

Signal is a potential and established indicator of new ADR. Signal is referred as any new possible causal link between a suspected ADR and drug; which is previously unknown or incompletely documented. It is generated by reported cases of ADRs. However, careful judgment and establishment of possible causal relationship is always warranted to exclude the misinterpretation

of the signal. Usually more than one report is required to generate a signal depending upon the seriousness of the event and quality of the information. A signal may not be definitive but it indicates the need for further enquiry or action. There are different sources of signal. Observation in patient, often called as qualitative signal, observation in population, often called as quantitative signal and the experimental findings are the main sources of signal. The widely Pharmacovigilance: An Overview 3 used methods to find out the signal are spontaneous reporting system (SRS), active surveillance, cohort studies, case control studies. SRS is the basic and most widely used method since decades to report ADRs. It can be used to identify rare ADRs however under-reporting remains the major limitation, accounts for 90-95%.

VACCINESANDBIOLOGICALMEDICINES: [41-43]

Vaccines and biological medicines require modified systems of safety monitoring. They are often administered to healthy children. This applies particularly to vaccines used within a national immunization program. In many countries, those exposed to a particular vaccine represent the entire birth cohort and therefore a sizeable part of the entire population. People's expectations of safety are high, and they are reluctant to countenance even a small risk of adverse events. Concerns regarding vaccine safety, real or imagined, may result in loss of confidence in the entire vaccine programs. This can result in poor compliance and a consequent resurgence in morbidity and mortality of vaccine-preventable disease. The difficulties in monitoring and dealing with vaccine safety are complicated by the problems inherent in determining the causal link between an adverse event following immunization and a vaccine. For example, information on dechallenge and rechallenge is often missing, and vaccines are given to most of the country's birth cohort at an age when coincidental disease is likely.

Several vaccines are likely to be administered concurrently. The possibility of programmatic errors should never be overlooked. A programmatic error is a medical incident that is caused byerrors in the transportation, storage, handling or administration of vaccines. However, the responsibility of the regulatory authority is by no means limited to the safety of vaccines used in immunization programs. Several biological products are used in specific patient populations as preventive or curative measures. The efficient regulation of these products is crucial in order to avoid potential harm to the public as a result of substandard manufacture or improper transportation and storage of imported vaccines and biological medicines. In recent years, the safety of biological products and blood products has come under public scrutiny. Concerns about the safety of medicinal products of animal origin have been raised in connection with variant Creutzfeldt-Jacob disease (vCJD) and with contamination of blood and blood products by infectious organisms such as HIV and hepatitis B. The quality of screening and sterilization procedures and appropriate selection of donors are linked to the risks of contamination. Such safety issues related to the use of plasma-derived medicinal products should fall under the aegis of PV programs. For that to happen, PV centers would have to consider the special issues related to safety of these products. Expertise in biological products, virology and medical microbiology would be required. Clinical trials in large patient populations are being considered for testing the efficacy and safety of biological medicine.

CLINICAL TRIALS IN INDIA: [44-55]

Global pharmaceutical companies have found India to be a preferred destination for clinical trials because India's clinical research space and opportunities are very attractive. Some of the advantages for clinical trials that India has as are as follows:

• High degree of compliance to international guidelines such as the International Conference on Harmonisation (ICH) / WHO Good Clinical Practice (ICH-GCP) and the regulations lay down by the US Food and Drug Administration.

• Availability of well qualified, English speaking research professionals including physicians.

• Ongoing support and cooperation from the government.

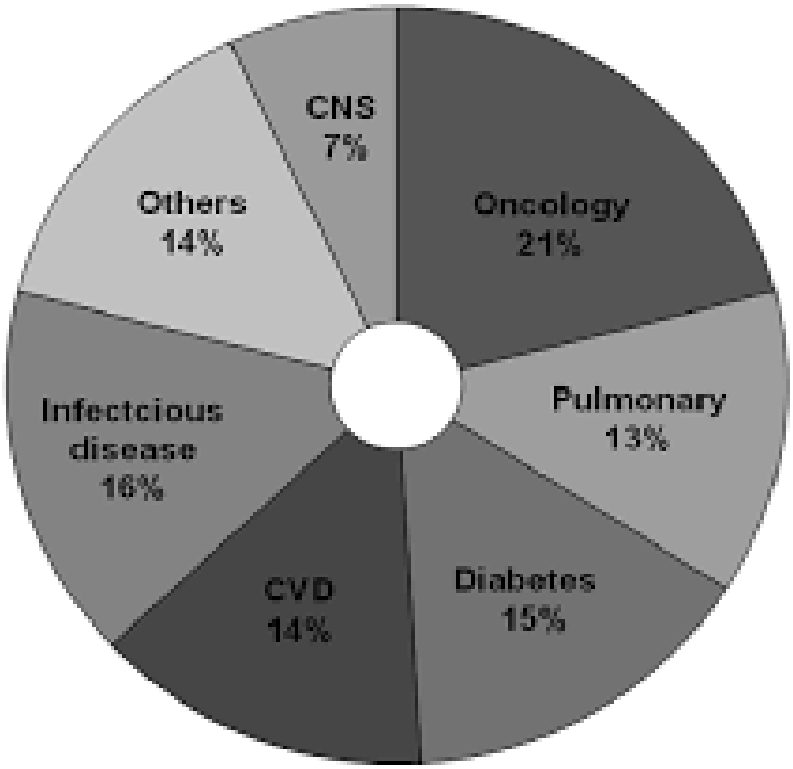
• Lower cost compared to the west.

• Increasing prevalence of illnesses common to both developed and developing countries.

• Availability of good infrastructure.

• Changes in Patent Laws since January 2005.

As per a recent report from Federation of Indian Chambers of Commerce and Industry (FICCI), scientific feasibility, medical infrastructure, clinical trial experience, regulations, commercialization potential and cost competitiveness are some of the growth drivers responsible for the metamorphosis of Indian clinical research in the recent past. Indian-born contract research organizations (CROs) were able to offer the advantages of understanding the Indian scenario better, provide services at more competitive costs, and having better knowledge of Investigator sites in the country compared to the newer entrants in the market. India’s existing favorable regulatory framework and regulations with international standards, increasing awareness of good clinical practice guidelines and its implementation by clinicians are some ofthe main reasons propelling the growth of clinical research in India. The therapeutic area wise distribution of clinical trials and availability of diverse patient population across major therapeutic segments in India.



SWOT Analysis of Indian Clinical Trial Sector

Strengths

• Large population of over 1.2 billion, about 16% of the world's population.

• Huge pharmaceutical and biotech industry base with availability of skilled persons.

• Third largest players in the world with 500 different active pharmaceutical ingredients.

• Currently accounts for 8% of global pharmaceutical production, being fourth in the world.

• Conducive initiatives to harness India's innovative capability by government.

• Huge data mining related to safety profile of drugs due to large population.

Weaknesses

• As per 2009-10 estimates, expenditure on health sector was 2.1% of the total budget and 0.35% of the Gross domestic product (GDP) of India.

• Developed countries like United States, France, Switzerland and Germany, spent around 16%, 11%, 10.8% and 10.4% of their GDP respectively.

• Less funding available for implementation of programs and issues of national importance such as PV.

Opportunities

• The Indian population is the largest source of human biodiversity.

• Consists of 4635 culturally and anthropologically well-defined populations, representing a perfect model to study efficacy, disease susceptibility, etiology, molecular pathology, and safety profile of drugs with respect to genetic diversity.

• Excellent potential for skilled human resources required for an effective PV system due to >300 medical, >230 dental, >830 pharmacy and >650 recognized nursing colleges in India.

Threats

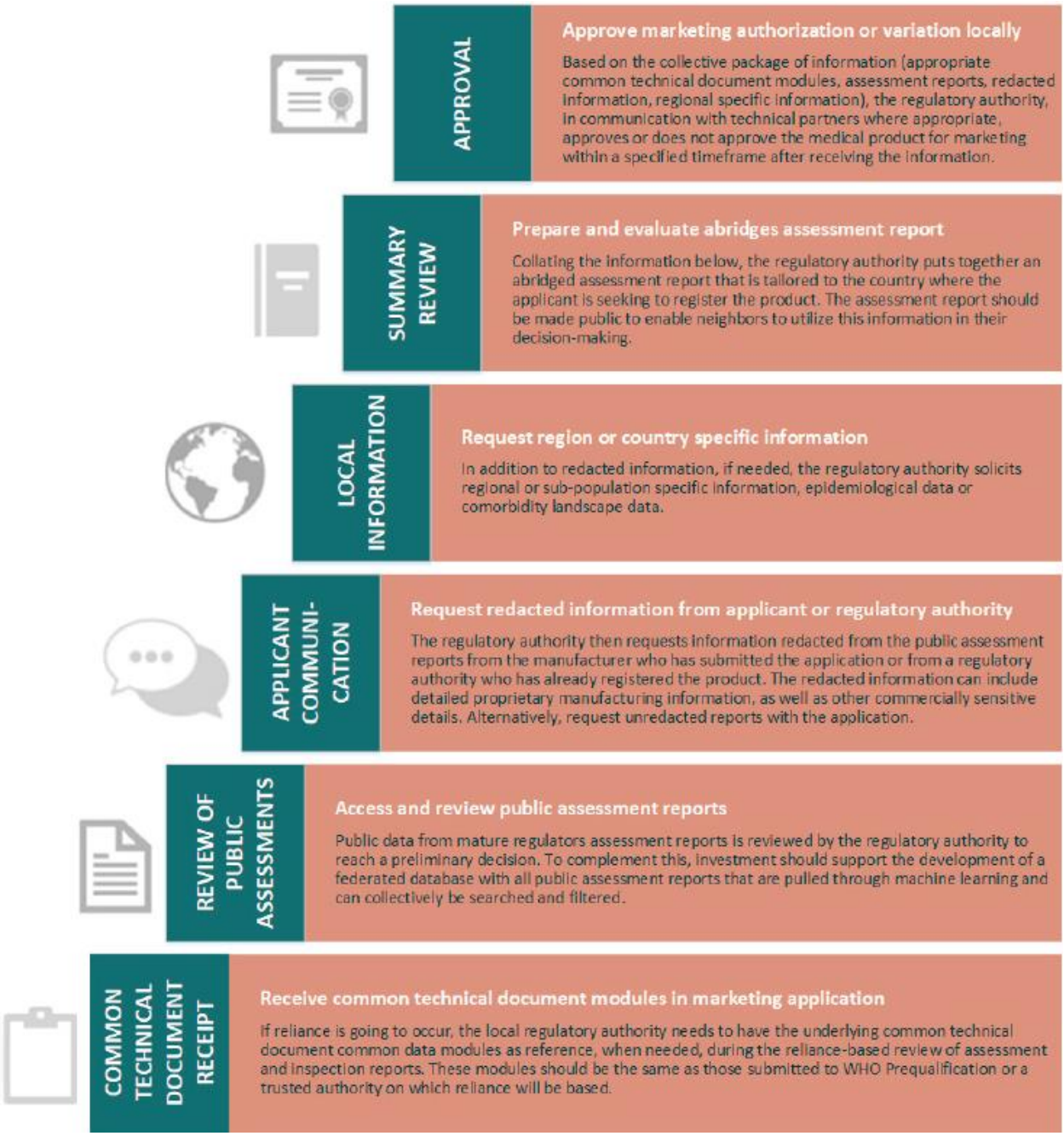
• Under reporting of ADRs.

• Low availability of funds.

• Less ADRs monitoring centers.

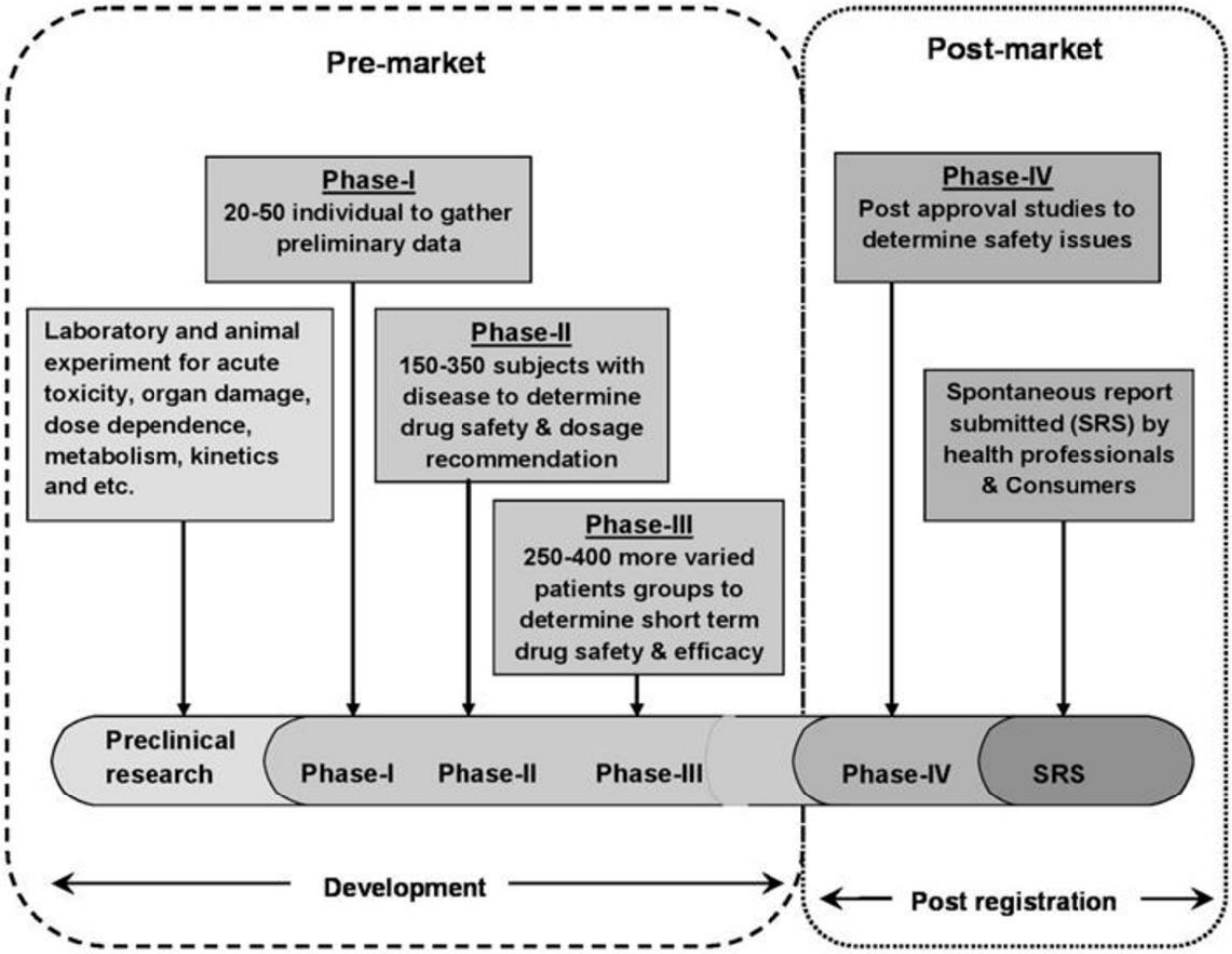
Agencies Involved for Clinical Research Regulation In India

Various regulatory agencies of India and their prominent roles in overseeing clinical trial along with Ethics committee



DATA MININGFOR PV: [56-67]

PV, also known as drug safety surveillance, is the science of enhancing patient care and patient safety regarding the use of medicines by collecting, monitoring, assessing, and evaluating information from healthcare providers and patients. In that view, PV can be divided into two stages such as premarketing surveillance – information regarding ADRs is collected from preclinical screening and phases I to III clinical trials; and post-marketing surveillance – data accumulated in the post approval stage and throughout a drug's market life.



PV has relied on biological experiments or manual review of case reports; however, due to the vast quantities and complexity of data to be analyzed, computational methods that can accurately detect ADRs in a timely fashion have become a critical component in PV. Large-scale compound databases containing structure, bioassay, and genomic information, as well as comprehensive clinical data sets such as electronic medical record (EMR) databases, have become the enabling resources for computerized ADR detection methods.

Premarketing surveillance

PV at the pre-marketing stage has been devoted to predict or assess potential ADRs early in the drug development pipeline. One of the fundamental methods is the application of preclinical invitro Safety Pharmacology Profiling (SPP) by testing compounds with biochemical and cellular assays. The hypothesis is that if a compound binds to a certain target, then its effect may translate into possible occurrence of an ADR in humans. However, experimental detection of ADRs remains challenging in terms of cost and efficiency. There have been numerous research activities devoted to developing computational approaches to predict potential ADRs using preclinical characteristics of the compounds or screening data. Most of the existing research can be categorized into protein target-based and chemical structure-based approaches. Others have also explored integrative approach.

Post-marketing surveillance

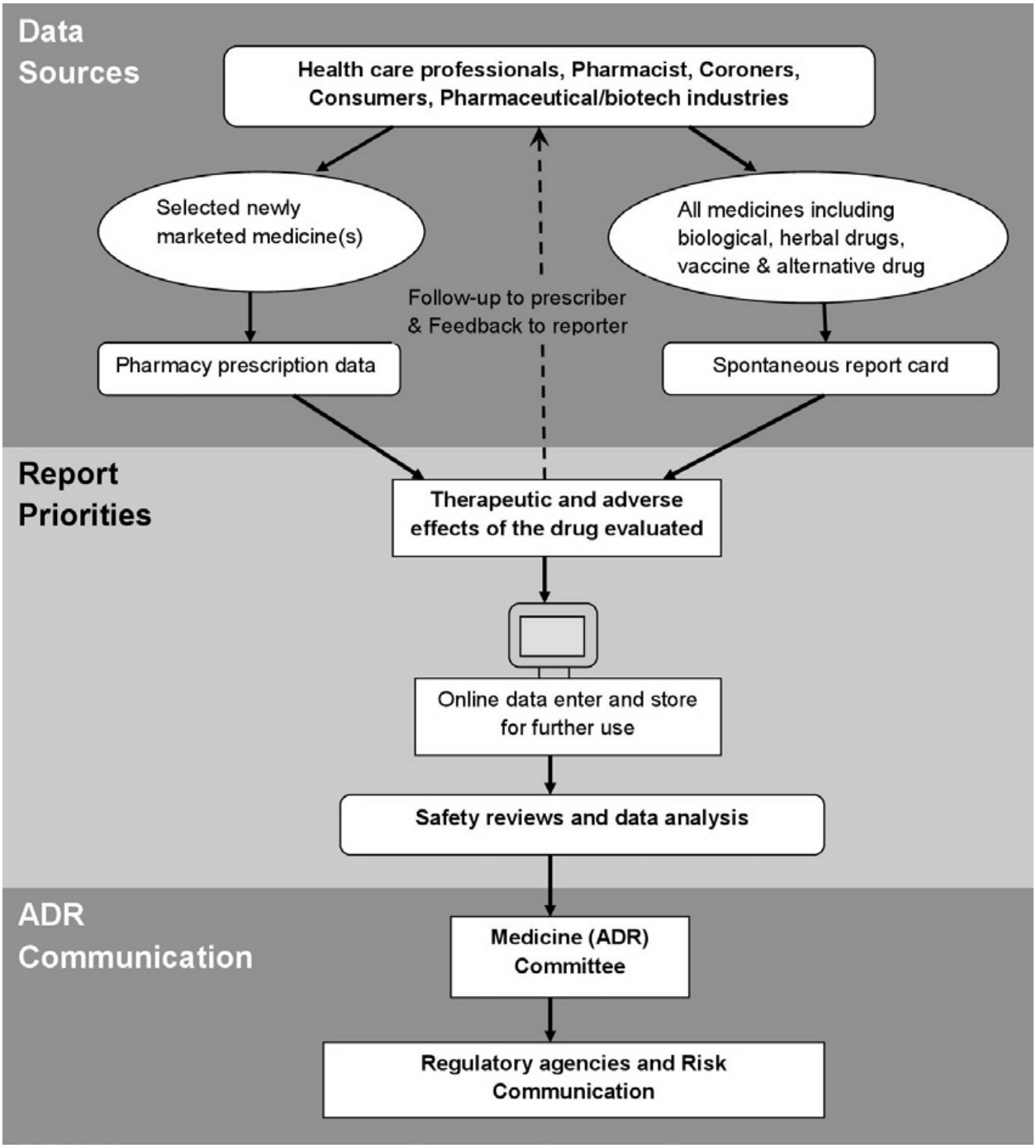
Although a drug undergoes extensive screening before its approval by the Food and Drug Administration (FDA), many ADRs may still be missed because the clinical trials are often small, short, and biased by excluding patients with comorbid diseases. Premarketing trials do not mirror actual clinical use situations for diverse (e.g. inpatient) populations, thus it is important to continue the surveillance post-market. PV plays an essential role in the post-market analysis of newly developed drugs. Pharmaceutical companies' competition along with rigorous regulatory evaluation procedures empowers a complex research and development process before launching a new drug into the market. Several unique data sources are available for post-marketing PV.

PV research is based on the analysis of "signals". The World Health Organization (WHO) defines signals as undisclosed assertions on direct relationships between effects on the human organism and a drug to induce adverse events. To generate comprehensive signal datasets, clinicians and researchers use spontaneous reporting systems (SRS). Electronic SRSs are already in place throughout some European countries and the United States. Likewise, other solutions, such as general practitioners' databases analysis, post market studies or prescription monitoring, among others, are being thoroughly explored. Nevertheless, the majority of data is not publicly available for researchers, which, jointly with other barriers, severely limits signal detection. Although drug companies are required to track and manage adverse events reported by clinicians, lawyers or patients, the detection process relies mostly on the physician's ability to recognize a given trait as a drug adverse event. Whereas the problem for collecting and filtering ADR data from multiple distributed nodes has already been studied in the past, researchers continue to pursue the best strategies to delve into the wealth of collected data in conjunction with other post drug administration inputs. With data and text-mining techniques scavenging millions of electronic medical records, PV researchers are now faced with the problem of delivering knowledge-oriented tools and services that exploit the scope of collected data. Ultimately, the adequate exploration of these data will pave the way for improved drug evaluations, critical for pharmaceutical companies, regulatory entities and researchers.

PV IN India: [68-71]

In India, consideration for the surveillance of ADRs developed relatively late, as traditionally there was no concept of surveillance of medicines in the country. Even though PV is still in its infancy, it is not new to India. It was not until 1986 when a few physicians, mainly from academic institutions, called for greater attention to be devoted to the potential adverse effects of prescription medicines and rational prescribing of medicines. This led to the formation of the first ADR monitoring program consisting of 12 regional centers, each covering a population of 50 million, but was unsuccessful. Nothing much happened until a decade later when India joined the WHO Adverse Drug Reaction Monitoring Programme based in Uppsala, Sweden in 1997. Three centers for ADR monitoring were identified, mainly based in the teaching hospitals. A National Pharmacovigilance Center located in the Department of Pharmacology, All India Institute of Medical Sciences (AIIMS), New Delhi and two WHO special centers in Mumbai (KEM Hospital) and Aligarh (JLN Hospital, Aligarh). These centers were to report ADRs to the drug regulatory

authority of India. The major role of these centers was to monitor ADRs to medicines marketed in India. However, they were non-functional as information about the need to report ADRs and about the functions of these monitoring centers never reached the prescribers and there was lack of funding from the government. This attempt was unsuccessful, and hence, again from 1 January 2005, the WHO-sponsored and World Bank-funded National Pharmacovigilance Program (NPVP) for India was formulated. NPVP structure



The NPVP, established in January 2005, was to be overseen by the National Pharmacovigilance Advisory Committee based at the Central Drugs Standard Control Organization (CDSCO). Two zonal centers, the South-West (SW) zonal center (located in the Department of Clinical Pharmacology, Seth GS Medical College and KEM Hospital, Mumbai) and the North-East (NE) zonal center (located in the Department of Pharmacology, AIIMS, New Delhi) were to collect the

information from all over the country and send it to the committee as well as to the Uppsala Monitoring Centre (UMC) in Sweden. Three regional centers would report to the Mumbai center and two to the New Delhi one. Each regional center, in turn, would have several peripheral centers (24 in total) reporting to it. The program had three broad objectives. The shortterm objective was to foster a reporting culture, the intermediate objective was to involve large number of healthcare professionals in the system in information dissemination, and the long-term objective was for the program to be a benchmark for global drug monitoring. However, this program also failed.

ROLE OF PHARMACIST: [72-75]

• Effective and safe pharmacological treatment process requires a team work of the patient and healthcare professionals. Pharmacists and nurses plays a crucial role in monitoring and identification of drug related problems; thus maintain safe use of medicines.

• Pharmacists contribute to the drug safety by preventing, identifying, documenting, and reporting of ADRs.

- To promote rational use of medicines by identifying whether the patients receive medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, cost effective etc.

- Pharmacist plays a vital role in medication safety monitoring.

- Pharmacists can assure a positive environment to the patients in minimizing the medication errors, improve patient safety and quality of life during the counselling session.

- Developing communication materials like newsletters and other publications through the drug information and poison centres, whichare utilized by the health care professions.

CONCLUSION:

The PV in India has become an important public health issue as regulators, drug manufacturers, consumers, and healthcare professionals are faced with a number of challenges. The PV in India continues to grow, evolve, and improve. India is the largest producer of pharmaceuticals and now emerging as an important clinical trial hub in the world. Apparently, the requirements for professional specialization, a combined view on PGx and clinical requirements are needed. Thathelps to identify factors that increase the risk of unwanted outcomes from drug therapy and prior to commencing drug treatment and in tailoring drug treatment for individual patients. The PV has also involved in Data Mining Technology in spontaneous reports submit to the national surveillance systems. The PVPI is coordinated at IPC through NCC under the control of Indian Government to generate an independent data on safety of medicines, which will be at par with global drug safety monitoring standards. National and regional PV systems are well-adapted bodies, attuned to the intricate collection and analysis of ADR data that leads to timely alerts and interventions to protect population health. Furthermore, it is responsible in India of entire campaign to improve PV knowledge and increase the number of ADRs reports up to the gold standard level established by the WHO.

The adverse events reported by PV system will potentially benefit to the community due to their proximity to both the population and public health practitioners, in terms of language and knowledge of the lifestyle and habits of patients, enables easy contact with reporters, for example by telephone, Email, text massages by mobile phones. The development of new and effective medicinal products makes a positive contribution to the health and well being of individuals. However, there is a need to improve PV systems to more effectively monitor and take action on safety issues associated with medicines to enhance their contribution to public health. Hence, PV for medicinal product safety to help the patients get well and to manage optimally or ideally, avoid illness is a collective responsibility of industry, drug regulators and clinicians and other healthcare professionals. The financial support and future projects should help to achieve a more comprehensive PV activity in India.

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