



REVIEW ON PHARMACOVIGILANCE

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Abstract: Medicines and vaccines play a crucial role in the prevention and treatment of a disease. Even after the drug has been approved for sale in the market, it may have certain unexpected or undesirable side effects. These side effects of the drugs need to be monitored, as a large number of people consume them. Pharmacovigilance helps to monitor the side effects and other related problems associated with medicines and vaccines.

Keywords: Pharmacovigilance, Clinical trials, ICH–Good Clinical Practices.

Introduction:

According to the World Health Organization, pharmacovigilance is the science related to detecting, evaluating, understanding, and preventing side effects of drugs and vaccines, or other related problems.^[1]

The primary goal of pharmacovigilance is to provide patients with certainty about their medicines. Because relatively few patients are selected in clinical trials, results regarding the safety and efficacy of drugs are limited, drugs are approved for use, and drugs are tested for a limited period. After approval, it can be used for many patients for a long time. As this drug is being used by more people, certain side effects may occur. This raises drug safety issues. Therefore, it is important to continuously monitor the safety of all medicines. Pharmacovigilance, therefore, plays an important role in monitoring the safety and efficacy of medicines.^[2]

Clinical Research:

A complete study of drug safety and efficacy. Volunteers participate to better understand medicines. All drugs, tools, diagnostic tests, devices, techniques, and techniques used in the medical field today were tested once on individuals who volunteered to participate in clinical studies. Both healthy and sick people can participate in clinical research. A participant is a person who chooses whether or not to participate in the study and can opt out of the study at any time for any reason.^[3]

Clinical Trials:

Research studies are conducted on people to evaluate medical, surgical, or behavioral interventions. A clinical trial is a way to see if a new drug, treatment, or medical device is safe and effective for human use.

Clinical trials have four phases:

Phase I: These trials study small numbers of healthy people (20-80) to determine drug safety and side effects and to find the correct dosage. Approximately 70% of drugs are moved for further testing.

Phase II: In this trial, the primary focus is on drug efficacy. More volunteers (100-300) will participate in Phase II. At the same time, safety and short-term side effects are also examined in these studies. Approximately 33% of drugs are eligible to proceed to Phase III trials for further study.

Phase III:

The Phase III trial will help gather more information about the safety and efficacy of in different populations, at different doses, and in combination with other agents. Hundreds to 3000 of them have voluntarily participated in these studies. If the FDA agrees that the study results are positive, the FDA will approve the experimental drug or device. Approximately 25-30% of drugs progress to the next phase.

Phase IV:

Phase IV trials are conducted when the FDA approves a drug for post-market safety studies. Thousands of volunteers suffering from illness are involved. The primary objective of the study is to monitor safety in large population groups. ^[4]

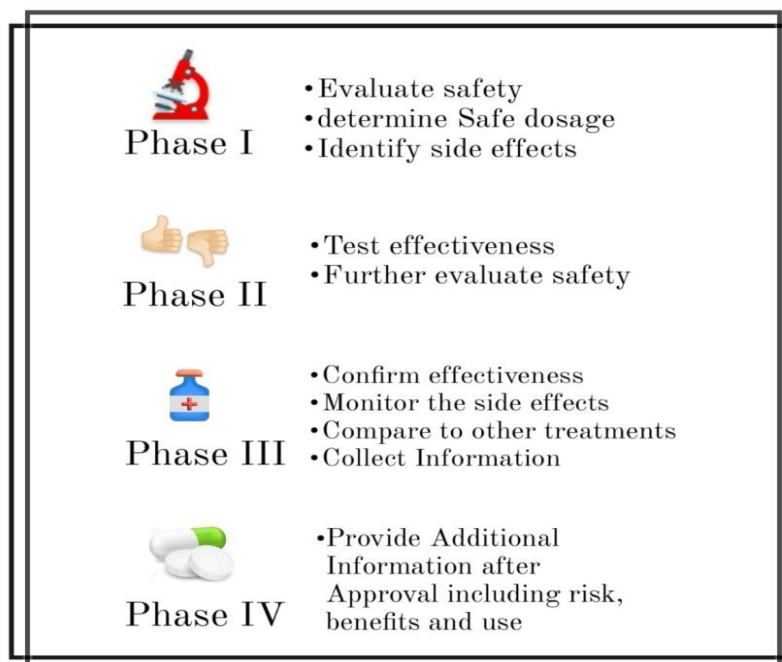


Fig: phases of clinical trials

Functions of Drug Controller General of India:

The Drug Control Authority of India (DCGI) is responsible for approving licenses in India for certain categories of drugs such as blood and blood products, vaccines, IV fluids, and serum. DCGI also sets standards for the manufacture, sale, importation, and distribution of medicines in India.

DCGI establishes standards and quality for the manufacturing, marketing, importing, and distribution of pharmaceuticals in India.

- Court of Appeals for Disputes Concerning the Quality of Pharmaceutical Products.
- Preparation and maintenance of national reference standards.
- To create uniformity in the implementation of the Drugs and Cosmetics Act.
- Training of drug analysts on behalf of state drug control laboratories and other agencies.
- Analysis of cosmetics obtained as research samples from CDSCO (Central Drug Standard Control Organization).^[5]

Functions of Central Drugs Standard Control Organization:

- New drug testing.
- Approval of new drugs and clinical trials.
- Import Registration and License.
- Blood Banks, LVPs, Vaccines, r-DNA Products, and Certain Medical Device License Approvals (CLAA Program).
- Amendments to D and C Laws and Regulations.
- Prohibition of Medicines and Cosmetics.
- Issuance of test licenses, personnel licenses, and NOCs for export.
- Oversight and market surveillance by the Center's supervisory authorities beyond national authorities.^[6]



Fig: functions of CDSCO

Types of Regulatory Applications Resources for IND Application:

➤ Investigational New Drug (IND) :

An Investigational New Drug Application (IND) is a request by a clinical trial sponsor for approval by the Food and Drug Administration (FDA) to administer an investigational drug or biologic to humans. Clinical trials are often conducted to gather safety and efficacy information to support marketing applications for biological and pharmaceutical products. Unless exempted, clinical trial sponsors must submit an IND to obtain FDA approval to conduct the trial. Such approval must be obtained before interstate transportation and administration of new drugs or biologics that are not the subject of an approved New Drug or Biologics application.

Extended access to products in development may be granted by the FDA as a compassionate measure. These INDs are intended for use in patients with serious illnesses outside of clinical trials when no comparable or satisfactory alternative treatment options are available, and qualified physicians determine whether the benefits outweigh the anticipated risks. [7]

➤ **New Drug Application (NDA) :**

A New Drug Application (NDA) is a vehicle for a drug sponsor to formally offer the FDA approval of a new drug for sale and marketing in the United States. The purpose of the NDA is to provide enough information for FDA to make its next important decision.

Whether the methods used to manufacture the medicinal product and the controls used to maintain the quality of the medicinal product are adequate to ensure the identity, strength, quality, and purity of the medicinal product. [8]

➤ **Abbreviated New Drug Application (ANDA):**

An abbreviated marketing authorization application (ANDA) contains data submitted to the FDA for possible review and approval of generic drugs. Once approved, applicants can manufacture and market generic drugs to provide a safe, effective, and inexpensive alternative to the related brand-name drug. A generic medicinal product is a medicinal product that is comparable to an innovative medicinal product in terms of dosage form, strength, route of administration, quality, performance characteristics, and intended use.

Generic drug submissions are called "abbreviated" because they are not required to include preclinical (animal) and clinical (human) data demonstrating safety and efficacy. Instead, generic drug applicants must scientifically prove that their product performs the same as the innovative drug. One method demonstrated by researchers is to measure the time it takes generic drugs to reach the bloodstream of healthy volunteers. This proof of 'bioequivalence' indicates the absorption rate or bioavailability of the generic drug and can be compared to the innovative drug. To receive FDA approval, the generic version must deliver the same amount of active ingredient into the patient's bloodstream in the same amount of time as the innovative drug. [9]

Good Clinical Practices:

Good Clinical Practice (GCP) is an international ethical and scientific quality standard. Adherence to this standard protects the rights, safety, and health of human subjects following the Declaration of Helsinki and the principles of reliability of clinical trial data.

Objectives of ICH GCP Guidelines:

The purpose of this ICH-GCP Guide is to provide common standards for the European Union (EU), Japan, and the United States to facilitate mutual recognition of clinical data by European regulatory authorities. These guidelines were developed based on the current good clinical practice of the European Union, Japan, the United States and Australia, Canada, Nordic countries, and the World Health Organization (WHO). Prospective clinical trial data should follow these guidelines when submitted to regulatory authorities. The principles outlined in this guide may be applied to research conducted in other clinics that may affect subject safety and health. [10]

Scope of ICH GCP Guidelines:

The purpose of this guidance is to outline the mission and organization of a sponsor's audit department and the principles of audit planning, conduct, and reporting. All of these should be considered when conducting audits of clinical trials conducted by sponsor auditors. This guidance, together with the International Conference on Harmonization (ICH) Good Clinical

Practices (GCP), is intended to be the guiding principle for sponsor auditors to conduct audits in a variety of countries and sponsor contexts. ^[11]

Concept of Pharmacovigilance:

Definition:

According to World Health Organization, Pharmacovigilance can be defined as ‘the science and activity related to the detection, evaluation, understanding, and prevention of side effects or another drug/vaccine-related problems. All medicines and vaccines undergo rigorous safety and efficacy testing in clinical trials before they are approved for use.’^[1]

Objectives:

Improving the care and safety of patients related to the use of medicines in medical and healthcare settings remains an important parameter. The main goals of pharmacovigilance include demonstrating the effectiveness of a drug by monitoring its adverse effect profile over many years from the laboratory to the pharmacy; tracking serious drug side effects to promote public health and safety related to drug use; promoting the safe, rational and economical use of drugs; Prior understanding, knowledge and clinical training in pharmacy; and effective public relations. ^[12]

Components of Pharmacovigilance:

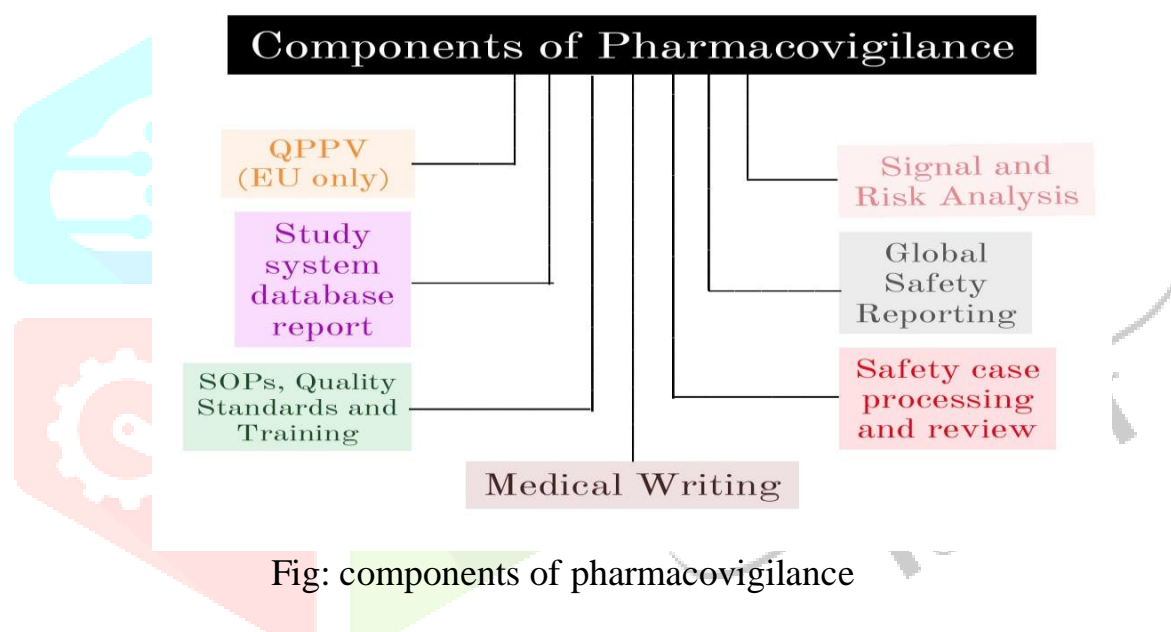


Fig: components of pharmacovigilance

Types of Pharmacovigilance:

- i. Passive monitoring
- ii. Monitoring is active
- iii. Case-control cohort
- iv. Targeted clinical trials

- **Passive monitoring:**

Passive surveillance methods include the use of spontaneous adverse event reports submitted voluntarily by healthcare professionals or patients to marketing authorization holders or regulatory authorities. Here, data on adverse reactions are collected in a central or regional database. The reporter's identity remains unknown, but patient-related details such as country, age, gender, and pre-existing conditions can be obtained from the report form. Examples of self-reporting systems include: FAERS (FDA Adverse Event Reporting System) database managed by FDA VigiBase™ is WHO's Global Personal Situation Safety Report (ICSR) database For Europe: EudraVigilance is maintained by the European Medicines Agency Currently, there is no specific self-reporting system for India. . authorized person to track and collect ICSR and online database in Vigi-Flow software)

- Active monitoring

This method aims to monitor specific adverse events related to drugs and attempts to determine the number of adverse drug reactions through a pre-planned process. It is usually called toxicity control or safety control.

- Cohort case-control

In this method, a monitoring plan is planned before starting treatment with drugs. A group of people are exposed to the drug at various times and are actively monitored during treatment. Adverse events from the target drug or events related to one or more drugs taken with that drug are monitored.

- Targeted clinical trials

This type of research is done to detect and characterize the adverse effects associated with drugs in special populations, such as people with genetic disorders, pregnant women, and the elderly. ^[13]

Constitutional Objective of Pharmacovigilance :

- Analyze the benefit-risk ratio in the market of medicine.
- Produce evidence-based information on drug safety.
- Create a nationwide system for patient safety reporting
- Support regulatory authorities in the decision process of using drugs.
- Provide safety information about its use of medicine to various stakeholders to reduce risks.
- Emergence as a national center of excellence in medicine.
- Work together with other national centers for data exchange and data management.
- Provide training and mentoring support to other national pharmacovigilance centers that are located across the globe.
- To identify and analyze the new signal (ADR) from the reported cases. ^[14]

List of ADR monitoring centres under pharmacovigilance program of India (PVPI)

1. Department of Pharmacology, Therapeutics & Toxicology, Govt. Medical College, Bakshi Nagar, Jammu.
2. Department of Pharmacology, PGIMER, Chandigarh
3. Department of Pharmacology, R.G. Kar Medical College, Kolkata
4. Department of Pharmacology, Lady Hardinge Medical College, New Delhi
5. Department of Clinical Pharmacology, Seth GS Medical College & KEM Hospital, Parel, Mumbai
6. Department of Clinical & Experimental Pharmacology, School of Tropical Medicine, Chittaranjan Avenue, Kolkata
7. Department of Pharmacology, JIPMER, Pondicherry
8. Department of Clinical Pharmacy, JSS Medical College Hospital, Karnataka
9. Department of Pharmacology, Medical College, Guwahati. Assam
10. Institute of Pharmacology, Madras Medical College, Chennai
11. Department of Pharmacology, SAIMS Medical College, Indore-Ujjain
12. Department of Pharmacology, GSVM Medical College, Swaroop Nagar, Kanpur, U.P.
13. Department of Pharmacology, Pandit Bhagwat Dayal Sharma, Post Graduate Institute of Medical Sciences, Rohatak, Haryana.
14. Department of Pharmacology, Dayanand Medical College and Hospital, Ludhiana, Punjab
15. Department of Clinical Pharmacology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J&K.
16. Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand

17. Department of Pharmacology, SMS Medical College, Jaipur

18. Department of Clinical Pharmacology, Christian Medical College, Vellore, Tamil Nadu.

[15]

Conclusion: Pharmacovigilance plays a crucial role in evaluating the safety and efficacy of the drugs, even after they are approved for sale in the market. Clinical trials are essential for determining the safety, efficacy and dosage of a new chemical entity. ICH-GCP improves the ethical awareness, trial concept and methods, public safety, cost effectiveness of research and development, competitiveness, data recognition and marketing structure.

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