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Review Article

Pharmacovigilance in India: Integration with Clinical Research, Regulatory Framework, and Global Harmonization

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ABSTRACT

Pharmacovigilance (PV) is critical for ensuring drug safety throughout the life cycle of medicinal products. In India, pharmacovigilance systems have been significantly shaped by evolving regulatory frameworks and increasing alignment with global standards. This review outlines the integration of pharmacovigilance with clinical research processes, elucidates key national regulations, and explores harmonized international guidelines. The integration of PV with clinical research procedures is highlighted in this study, with a focus on its relationship to post-marketing monitoring, clinical trial stages, and investigational new drug (IND) applications. It examines how important regulatory bodies like the IPC, DCGI, and CDSCO can put in place efficient drug monitoring systems. In order to improve data dependability, safety reporting, and risk management, the essay also addresses the need for harmonization with international frameworks created by ICH and WHO.

INTRODUCTION

Definition of Pharmacovigilance

Pharmacovigilance is the science and practice of recognizing, evaluating, analyzing, and avoiding other medication-related issues including adverse drug reactions (ADRs). The phrase "pharmacovigilance," which is derived from the terms "Pharmakon" (medicine) and "vigilance" (vigilance), emphasizes the importance of continuing to monitor medications after they are

introduced to the market. Although their use is limited, Clinical trials are crucial for assessing the safety and effectiveness of medications^[1].

Scope of Pharmacovigilance

The scope of pharmacovigilance is global and covers all aspects of the use of pharmaceutical products, from their development through to their marketing and use in clinical practice.

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The following are some of the key areas where pharmacovigilance has a significant impact:

Drug Development: Pharmacy supervision plays a key role in the development of new drugs by providing information on the safety profiles of new treatment methods and guides on the risks and benefits of these treatments.

Post-marketing Surveillance: Once a drug is on the market, pharmacovigilance activities continue through post-marketing surveillance, which involves the ongoing monitoring of the safety of drugs and the identification of harmful drugs, and will continue through post-operation observations.

Risk Management: Pharmacovigilance activities contribute to the development of drug risk management plans which aim to minimise the risk of harm to patients and ensure the safe use of drugs.

Regulatory Approval: The results of pharmacovigilance activities can inform regulatory decisions, such as drug approval or rejection of a drug from the market, or changes to the labelling of a drug.

Patient Safety: The Ultimate goal of pharmacovigilance is to increase patient safety; ensure the drug benefits outweigh the risks and prevent or minimise damage to patients [2].

History of Pharmacovigilance

When we call this the tale of a pharmacy director, it needs to be split into two parts. Tragedy before the pre-thalidomide era against the supervision of the pharmacy and the tragic post-thalidomide pharmacy. The tragedy of thalidomide was an event that led to the creation of modern pharmacology. Until the early 1960s, when these tablets were adopted by pregnant women for morning illness, normal anti-limen tablets resulted

in catastrophic and undesirable responses in newborns.

Pre-Thalidomide Tragedy Pharmacovigilance

Before the thalidomide tragedy, the regulatory authorities were working submissively for the safety of medicines, much like in reactive mode. The steps taken for drug safety or patient safety were merely the reaction to a particular event that happened in history and not an initiative-taking step to minimise adverse effects before the launch of medicine on the market. When a 15-year-old girl died, *The Lancet*, a prestigious scientific research publication house at the time, urged physicians to report anaesthesia-related deaths in Britain. Ensure the safety and purity of biological products, such as vaccinations and serums, the United States passed the Biological Control Act in 1902. The incident in 1901 that prompted the creation of this act involved the injection of tainted diphtheria antitoxins, which resulted in the deaths of thirteen children [3,4].

Thalidomide Tragedy

In the 1950s, the only non-barbituric sedative on the market was thalidomide. In 1954, the German pharmaceutical company Grünenthal made an accidental synthesis of it. Grünenthal conducted a quick clinical trial on people for sedation following preclinical research on rats and discovered that it caused sleep in humans. Using the slogan "completely safe in all", Grünenthal advertised the medication over the counter. Grünenthal said, "Unknown," when doctors enquired about its effect on the foetus. Peripheral neuropathy was the first significant side effect of thalidomide that long-term users experienced; however, they denied this assertion, stating that it was uncommon and that it could be reversed if halted. In the meanwhile, an Australian doctor found that thalidomide helps with morning



sickness and started giving off-label prescriptions for morning sickness to his pregnant patients and started the practice of giving pregnant women thalidomide for the same condition. In 46 countries where thalidomide was marketed, reports began to surface in the late 1950s and early 1960s that newborns had severe limb malformations, including shortness of both upper and lower limbs, and possessed the hallmarks of phocomelia. These limb deformities were noted in the offspring of mothers who had taken thalidomide during the second month of pregnancy. According to the doctors, these mums had consumed a teratogenic substance while pregnant. However, thalidomide is suspected of being responsible for this severe side effect. Grünenthal rejected its affiliation, but they were forced to halt its distribution in Germany, and most nations eventually outlawed it. Thousands of babies were born with serious birth abnormalities because of the hypnotic and antiemetic effects of the drug thalidomide. This incident underlined the importance of systemic monitoring of drug safety. The fallout raised awareness of the possible risks of medications, particularly during pregnancy [5,6].

WHO International Drug Surveillance

Soon after the thalidomide tragedy, the World Health Organisation (WHO) initiated concerted global efforts to address the issue of pharmaceutical safety.

The 16th World Health Assembly endorsed the resolution, which reaffirmed the need for responding promptly to reports of adverse drug reactions.

In order to develop a worldwide applicable system to monitor and detect adverse drug responses that had not yet been recognised, the WHO initiated a pilot project on international drug monitoring later in 1968. The pharmacovigilance principles and

procedures were implicated in this WHO step, and through systematic postmarketing surveillance conducted by national pharmacovigilance institutes, global data on adverse drug reactions (ADRs) from patient files was reported to the central database of the ADR of WHO [6].

Importance of Pharmacovigilance in public health & drug development

Early Detection of Adverse Drug Reactions (ADRs): Pharmacovigilance assists in detecting uncommon, severe, or unidentified side effects that might not be detected in clinical trials because of small sample sizes.

Improving Patient Safety: Continuous monitoring ensures that harmful drugs are withdrawn or their usage restricted, thereby preventing large-scale public health crises.

Promoting Rational Use of Medicines: PV data guides healthcare providers to prescribe drugs more safely, reducing medication errors and misuse.

Building Public Trust: A transparent and active PV system increases confidence in healthcare systems and drug safety.

Global Disease Control: Pharmacovigilance monitors events after vaccinations (AEFI) to guarantee safe immunisation practices in vaccination programmes.

Post-Marketing Surveillance (Phase IV): After drug approval, PV provides real-world data on long-term safety, effectiveness, and rare ADRs.

Regulatory Decision-Making: Data from PV influences labelling updates, warnings, restrictions, or even drug withdrawal.



Improvement of Clinical Trial Designs: Safety signals detected post-marketing can guide future trial protocols.

Supporting Innovation: By ensuring drug safety, PV fosters innovation and accelerates the development of safer therapeutic options.

Pharmacoeconomics: PV data can be used to assess the cost-effectiveness of medicines, especially when ADRs increase healthcare costs [7,8].

Need for robust regulatory system

a) Ensuring Safety, Efficacy, and Quality:- Regulations guarantee that medications undergo thorough clinical trials, preclinical investigations, and post-marketing monitoring prior to being available to patients. This prevents the distribution of substandard, falsified, or counterfeit drugs.

b) Protecting Public Health:- By tracking adverse drug reactions (ADRs) and managing product recalls, regulatory authorities serve as protectors of patient safety. Example: -The thalidomide tragedy in the 1960s and the withdrawal of Forecoxa in 2004 underscored the importance of stringent oversight.

c) Facilitating Innovation and Drug Development:- A robust regulatory framework motivates pharmaceutical firms to invest in research and development by providing predictable approval processes. It encourages the use of contemporary methods such as adaptive trials, pharmacogenomics, and personalised medicine.

d) Global Harmonisation:- Entities like the International Council for Harmonisation (ICH) and the World Health Organisation (WHO) stress the importance of standardised regulations to promote global drug development and

international commerce. A powerful system guarantees adherence to global standards, enhancing the worldwide availability of medications.

e) Combating Antimicrobial Resistance (AMR) and Misuse:- Regulations inhibit irrational prescriptions and over-the-counter misuse while ensuring responsible antibiotic use.

f) Strengthening Pharmacovigilance and Post-Market Surveillance:- Regulatory agencies such as the USFDA, EMA, and CDSCO (India) require ongoing safety assessments through pharmacovigilance. The early identification of risks facilitates updates to labels, restrictions on usage, or the withdrawal of unsafe products [9,10].

Necessity for harmonisation with global guidelines (ICH, WHO)

The global integration of pharmaceutical research and healthcare has generated an urgent demand for standardised guidelines. This harmonisation guarantees that medications are safe, high-quality, and efficient, while reducing the need for redundant regulatory processes and facilitating quicker patient access to innovative treatments.

a) Ensuring Global Public Health Protection Harmonized guidelines play a crucial role in maintaining uniform standards for drug quality, safety, and efficacy across various nations. The World Health Organization (WHO) establishes international standards for the safety of medicines, vaccines, and pharmacovigilance, particularly benefiting low- and middle-income countries.

b) Drug development and approval are made easier by the International Council for Harmonization's (ICH) guidelines for Good Clinical Practice (GCP), Quality (Q-series), Safety (S-series), and Efficacy (E-series). These guidelines establish

uniform standards for various regions, such as the US, EU, and Japan. This standardization reduces delays in clinical trials and regulatory filings across several nations and helps prevent duplicate research.

c) Encouraging Innovation and Faster Access Harmonization allows pharmaceutical companies to create a single global dossier that is acceptable to various regulatory authorities. This process speeds up patient access to life-saving treatments, as demonstrated by the rapid deployment of COVID-19 vaccines, which adhered to the WHO's Emergency Use Listing (EUL).

d) Strengthening Pharmacovigilance, The WHO's Uppsala Monitoring Centre (UMC) is responsible for coordinating the global reporting of adverse drug reactions (ADRs). The implementation of harmonized reporting standards, such as the ICH E2 series, enhances the detection of signals and ensures prompt action regarding drug safety.

e) Promoting International Trade and Collaboration Uniform technical requirements help to lower regulatory obstacles, thereby encouraging collaboration among nations. This approach supports the expansion of global markets for generics and biosimilars by ensuring adherence to international quality standards [9].

Clinical Research and regulatory system in India

Clinical research is a systematic study that uses human participants to produce data to identify or confirm clinical medicinal elements, such as pharmacodynamics and pharmacokinetics, along with any side effects, to evaluate the efficacy and safety of novel medications. A particular type of clinical study that follows a set methodology is represented by a clinical trial. People can take a more active approach to their healthcare, obtain

access to innovative treatments, and further medical research by taking part in clinical trials.

These studies are conducted with real patients in accordance with a predetermined strategy intended to evaluate cancer treatments, novel drug safety, and the efficacy of different human treatments.

Phases of clinical trial

Phase 1 (First in human trials)

In this stage, a group of healthy individuals, usually consisting of 20 to 80 participants, are chosen to receive the medication. The emphasis in this context is on evaluating both the effectiveness of the medication and any side effects it may induce in patients.

Phase 2 clinical trial (Therapeutic Exploratory)

This phase encompasses around 100 to 300 participants. Its focus is to examine the drug's efficacy in identifying medical conditions in individuals. Concurrently, safety evaluations are conducted, with a greater emphasis placed assessing the side effects encountered by participants.

Phase of 3 Clinical trial (Therapeutic confirmatory)

Enrolment rises to 1,000 to 3,000 subjects during this stage. The investigation persists in evaluating both safety and effectiveness but now encompasses a wider demographic and different dosages. Should regulatory authorities, like the FDA, grant approval for the drug based on positive trial results, it advances to the final phase.

Phase 4 Clinical Trial (post-marketing surveillance)

Following the approval by the FDA, many individuals opt to take part in clinical trials because existing medications or treatments may not be effective. Others may choose to enrol when there is no available cure for their condition. Participants frequently could experience cutting-edge therapies that have not yet been introduced to

the market. Furthermore, some individuals participate in these studies to support researchers in furthering their investigations. A variety of research initiatives focus on preventing certain diseases, including genetic disorders, especially within healthy populations^[10,11].

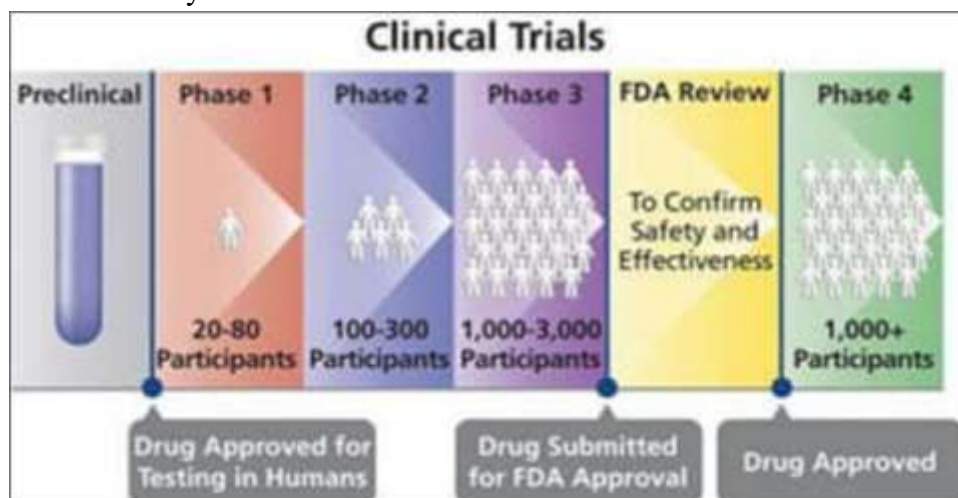


Figure no.1 Phases of Clinical Trial^[13]

Role of Regulatory Authorities

Drug Controller General of India (DCGI)

DCGI stands for the Drugs Controller General of India.

The GI is in charge of the Central Drugs Standard Control Organization (CDSCO), which operates under the Indian government.

In India, this body is in charge of granting licenses for specific medication categories. Additionally, the DCGI oversees the sale, import, production, and distribution of medicines in the nation and establishes crucial criteria and quality controls for them. Ensuring consistency in the enforcement of the Drugs and Cosmetics Act is one of its primary objectives.

The DCGI is in charge of the Central Drugs Standard Control Organization of the Ministry of Health and Family Welfare (CDSCO). The Drugs

and Cosmetics Act of 1940 is the source of the authority's authority. Under the auspices of CDSCO and DCGI, the Pharmacovigilance Program of India (Pvpi) was founded in 2010. Pvpi seeks to improve medication safety in India by gathering, tracking, and analyzing adverse drug reactions (ADRs). In India's healthcare system, this function is essential, particularly when it comes to the approval of medications and vaccines. The COVID vaccine approval procedure was recently greatly aided by the DCGI. It regulates the sale, importation, production, and distribution of medicines in India and establishes the essential requirements and quality benchmarks. It also controls pharmaceutical and medical standards^[11,12].

Responsibilities

1. The DCGI is tasked with the preparation and maintenance of essential reference standards for pharmaceuticals. It guarantees the uniform

enforcement of the Drugs and Cosmetics Act of 1940.

2. Furthermore, the DCGI evaluates cosmetics as part of a sample survey received from the Central Drugs Standard Control Organisation.
3. Acting as the primary licensing authority under the Medical Device Rules of 2017, the DCGI oversees the licensing of medical devices regulated by this legislation.
4. It provides approvals for pharmaceuticals in accordance with the Drugs and Cosmetics Act.
5. The DCGI has the responsibility for supervising the execution of clinical trials and setting standards for pharmaceuticals.
6. It also guarantees quality control for medications brought into the country.
7. The organisation collaborates with various state drug control agencies.

Central Drugs Standard Control Organization (CDSCO): Structure and functions

India's National Regulatory Authority (NRA) for pharmaceuticals and medical goods is the Central Drugs Standard Control Organization (CDSCO), which is run by the Ministry of Health & Family Welfare. The CDSCO operates in accordance with the Drugs and Cosmetics Act of 1940 and the regulations established in 1945, sharing regulatory duties with both central and state authorities for the oversight of drugs and cosmetics. CDSCO is committed to ensuring that all medical products used in India are safe, effective, and of high quality. It strives to maintain transparency, consistency, and accountability in its operations.

Among the primary responsibilities of CDSCO are: -

1. Approving new pharmaceuticals
2. Supervising clinical trials
3. Establishing standards for medications

4. Collaborating with State Drug Control Organisations to ensure uniform application of regulations across the nation.

Furthermore, in conjunction with state regulators, CDSCO grants licences for essential medicines such as:

Blood and blood products:

1. IV fluids
2. Vaccination
3. Sera^[14].

Investigational New Drug (IND)

An investigational new drug application (IND) is a request for authorization from the Food and Drug Administration (FDA) to administer an experimental drug or biological (serums, vaccinations, antitoxins, antigens, etc.) to humans.

Any new drug that is not covered by an authorized new drug application (NDA), abbreviated new drug application (ANDA), or product license application (PLA) must have such authorization obtained before being shipped or administered over state lines.

Manufacturers, who are usually sponsors, and medical professionals, who are usually investigators, are the two organizations that file many INDs. In some situations, people are allowed to fund their own research.

It should be easy for the commercial maker to determine whether to submit an IND [15].

IND Types

- Investigator IND application
- Emergency Use IND application
- Treatment IND application
- Screening IND application



Investigator IND application:-

This involves a doctor applying, starting, and conducting an investigation, and immediately directing the administration or dispensing of the investigational medication. A doctor may apply for a research IND to suggest investigating:

- An unapproved drug
- An approved product for a new indication or
- An approved product in a new patient population.

Emergency Use IND application: -

In accordance with 21 CFR, Sec. 312.23 or Sec. 312.20, this application enables the FDA to approve the use of an investigational medication in an emergency that does not permit time for the filing of an IND application. Additionally, it is used to patients who do not fit the requirements of an approved study protocol or in the absence of one. In this situation, the FDA may approve the drug's shipping for a designated use prior to the filing of an IND application.

Treatment IND application: -

This application is made for experimental drugs that are showing promise in clinical testing for serious or immediately life-threatening disorders, as the last clinical work is finished and the FDA assessment is in progress. A medicine that is not yet licensed for commercial use may be undergoing clinical testing for a serious or immediately life-threatening medical disease for people for whom there is no suitable or equivalent alternative pharmaceutical or other therapy.

Screening IND application:-

Find the desired compounds or formulations, it is filed for several similar compounds. It is possible to develop the desired chemical under a different IND. Additionally, it can be used to screen for various salts, esters, and other drug derivatives that have similar pharmacodynamics but differ chemically [16].

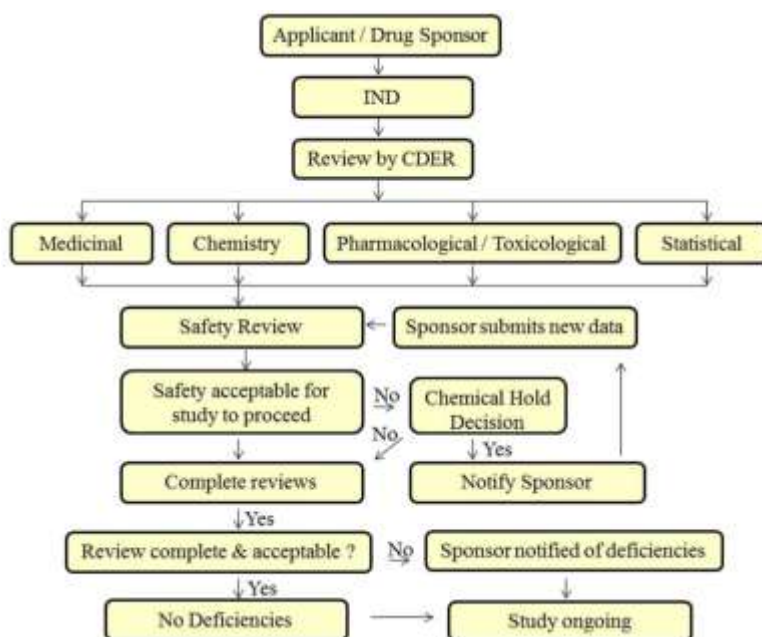


Figure no.2 Investigational New Drug [17]

New Drug Application (NDA)

The New Drug Application (NDA) has been used for many years to regulate and oversee new medications in the United States. Every new medication has needed an authorized NDA before it may be sold in the United States since 1938. Drug sponsors formally ask the FDA for permission to sell and promote a novel medication in the US through the NDA application. The NDA includes the data gathered from an Investigational New Drug's (IND) human and animal clinical trials^[18].

Functions of New Drug Application

1. Compile comprehensive data on a new pharmaceutical product, including preclinical and clinical testing.
2. Regulatory Submission: A formal request to regulatory bodies for authorization to sell the medication.
3. Extensive Evaluation: Regulatory bodies evaluate the production, safety, and effectiveness data.
4. Making Decisions: Authorities decide whether to accept or reject the New Drug Application (NDA).
5. Labelling Approval: This involves approving the drug's proposed label and providing usage guidelines.
6. Monitoring After Marketing: Following licensure, the medication's efficacy and safety are continuously monitored.
7. GMP Adherence: To guarantee constant product quality, approval signifies adherence to Good Manufacturing Practices.
8. Public Health Protection: - Guarantees that only safe and effective medications are available in the market, thereby reducing risks.

9. Supporting Innovation: - Establishes a route for groundbreaking drugs to meet medical requirements and be accessible to patients^[19].

Abbreviated New Drug Application (ANDA)

Drug goods (such as generics) that replicate drugs previously approved under a full NDA are typically subject to an abbreviated NDA (ANDA). Reports of clinical and nonclinical laboratory research are not necessary for an ANDA, except for those that deal with the drug product's in vivo bioavailability. When the FDA has decided that the information currently available is sufficient to prove that a certain drug's dosage form satisfies the legal requirements for safety and efficacy, the information may be left out. Products containing identical active ingredients, dosage forms, routes of administration, strengths, or conditions of use-manufactured by various manufacturers-are commonly referred to as duplicates^[19].

Key Facts Regarding Generics and the Generic Drug Application:

Applications for generic drugs are called "abbreviated" since they frequently don't need preclinical (animal) and clinical (human) evidence to prove efficacy and safety.

The time it takes for the generic medication to enter the bloodstream in 24 to 36 healthy volunteers is frequently used to determine bioequivalency; generic applicants must provide scientific proof that their medication is bioequivalent to the innovator medication, meaning it functions similarly to the innovator medication.

This assessment provides data on the bioavailability and rate of absorption of the generic medication, which may be compared to the innovator medications.



The "Drug Price Competition and Patent Term Restoration Act of 1984," also known as the "Hatch-Waxman Act," established the framework for the approval of generic drug copies.

The generic version must deliver an equivalent quantity of active ingredients into a patient's bloodstream within the same time as the innovator drug [20].

This is an application for the manufacturing of generic medications. The sponsor is not obliged to carry out any kind of clinical research or testing throughout this process. A generic medication producer must demonstrate that their product is bioequivalent to and similar to the previously approved brand product. An example of the ANDA approval procedure has been provided.

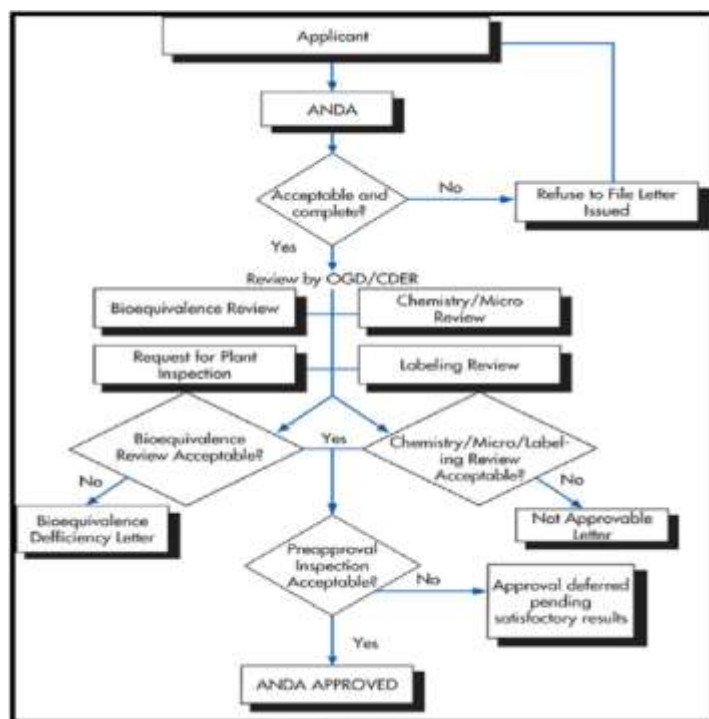


Figure no.3 Abbreviated new Drug (ANDA) [21]

Good Clinical Practices and Trial rules

A high-quality, ethical, and scientific worldwide standard for conducting studies involving human subjects is Good Clinical Practice (GCP). The purpose of clinical trials that follow this standard is to protect the rights, safety, and welfare of participants; to stay consistent with the Declaration of Helsinki's guiding principles; and to assure the validity of the trial findings. The phrase "trial conduct" refers to all procedures in this document, including planning, starting, conducting, documenting, supervising, evaluating, analysing, and reporting as needed. This ICH GCP

Guideline aims to provide a common standard that makes it easier for relevant regulatory bodies in ICH member nations and regions to receive clinical trial data from one another. ICH E8(R1) General Considerations for Clinical Studies provides the fundamental ideas upon which this guideline is based. A proportionate risk-based strategy, identifying essential elements for trial quality, proactively integrating quality into clinical trials and drug development planning, cultivating a quality culture, and engaging pertinent stakeholders as needed are all emphasized. Clinical trials vary in size, complexity, and expense. Analysing each trial's crucial quality

characteristics and the risks associated with them in detail will increase efficiency by focusing on tasks that are necessary to meet the trial's goals.

New Drugs and Clinical Trial Rules, 2019

On March 19, 2019, the New Drugs and Clinical Trial Rules 2019 were announced. Their goal is to create a reliable, understandable, and uniform framework for clinical studies. These rules are intended to provide Indians speedier access to new medications and clinical trials. "Academic Clinical Trials" refer to clinical trials of drugs that have already received approval for a particular application. This trial is conducted by an investigator, academic institution, or research organization for a new indication or method of administration. The outcomes of such a trial should not be utilized for marketing or commercial objectives. Typically, academic clinical trials are conducted to evaluate the safety, efficacy, and cost-effectiveness of a specific drug or treatment in a broader patient population^[23].

Objective of New Drugs and Clinical Trial Rules, 2019

The updated regulations feature a time-sensitive assessment of Applications and provide enhanced flexibility for researchers. Their purpose is to foster clinical research while ensuring predictability and accountability within the regulatory framework.

- The main objective is to advance research and development in India.
- Accelerated access to new medications.
- Predictability and transparency in the approval process.
- Decrease costs and reduce healthcare expenditures.
- Uphold the integrity of data, the safety and welfare of trial participants, and the quality

assurance of clinical research conducted in India.

Provision for Accelerated approval and orphan drug

Orphan medications are defined by the new legislation as "medication designed to address a condition that impacts no more than 500,000 individuals in India." Phase III and phase IV trials are exempt for orphan medications, according to this legislation. For certain treatments, an expedited review process is put in place, and the application cost is eliminated, helping Indians create more therapies to address uncommon medical diseases^[23].

Protocol designing and CTA Process

The design of a clinical trial protocol is a crucial step in the development and implementation of clinical research, acting as the essential framework for the entire study. A well-crafted protocol includes vital elements, detailing the study's goals, methodologies, eligibility requirements, treatment strategies, and data analysis methods. The main objective is to uphold both the scientific and ethical standards of the trial, enabling the production of reliable and significant data that enhances medical knowledge and guides healthcare decisions. Creating a protocol for a clinical trial is a significant undertaking that outlines the strategy for conducting the research in a structured and scientifically valid way. Below is a summary.

- Learning objectives: Articulate the primary and secondary goals of the trial. These goals direct the entire study and assist in evaluating the success or failure of the intervention.
- Study population: Define the traits of participants who are eligible to take part in the trial, including criteria for inclusion and



exclusion. This guarantees that the study population is uniform and allows for meaningful conclusions to be drawn.

- Intervention: A comprehensive description of the research outcome or intervention being investigated, encompassing measurement, administration method, duration, and comparison or control group
- Study design: Specify the trial type (e.g., randomized controlled trial, observational study), allocation ratio, blinding method, and randomization technique used^[24].

Key components of a Clinical trial protocol

The protocol's thoroughness encompasses information regarding the scientific rationale, objectives, study design, participant eligibility criteria, and treatment strategies. Furthermore, it delineates the statistical techniques for data analysis, ethical considerations, and the processes established to guarantee data integrity and participant safety. Moreover, the protocol details the responsibilities of organizations such as the Data Safety Monitoring Board (DSMB), the policy for publication, and the anticipated timeline for the trial. These elements collectively direct the execution of the study, ensuring uniformity,

adherence to ethical standards, and scientific rigor [25,26].

CTA Process

The application or submission submitted to the appropriate National Regulatory Authority in order to secure authorization for carrying out a clinical trial inside that nation is known as a Clinical Trials Application (CTA). Examples of submissions to appropriate National Regulatory Authorities include, but are not restricted to:

1. According to Title 21, Code of Federal Regulations, Part 312, an Investigational New Drug (IND) application must be filed with the U.S. Food and Drug Administration (FDA) for research carried out in the country.
2. According to Article 9(2) of Directive 2001/20/EC, a clinical study must be authorized inside the European Union (EU) by submitting an application to the relevant National Regulatory Authority.
3. A similar application or submission must be submitted to the relevant National Regulatory Authority in nations or areas outside of the United States and the European Union.

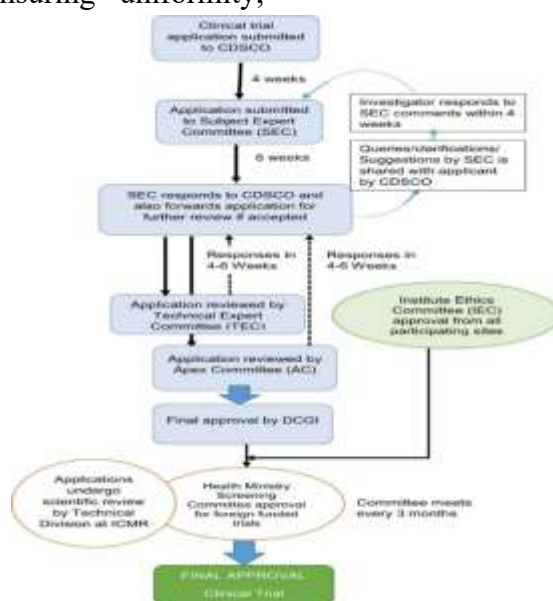


Figure no.4 CTA Process [26]

Fundamentals of Pharmacovigilance

Pharmacy oversight is recognized by both the International Council and World Health Organization (WHO) of Harmony (ICH) as an important scientific and regulatory field focused on promoting drug safety and effective use. Although their definitions are consistent, each organization emphasizes the various components of this area. The WHO (2024) describes drugs as "science and activities connected to identifying, evaluating, comprehending, and averting detrimental effects or other issues associated with the drug.

Monitoring Adverse Effects: Continuous observation aimed at identifying and evaluating negative side effects of drugs (ADRs) that can occur while taking medication.

Evaluation of Risk and Benefits: Examining the balance between the risks and advantages of drugs to ensure that the therapeutic advantages outweigh any possible dangers or negative consequences.

Risk management and mitigation: Creating plans to address and reduce hazards related to pharmaceuticals, such as changing labels, putting risk-reduction techniques into practice, or, if required, removing pharmaceuticals from the market.

Promoting Safe Medication Practices: Educating patients and medical professionals on how to take pharmaceuticals safely and effectively, including proper dosage, delivery techniques, and monitoring [27].

Types and Components of PV

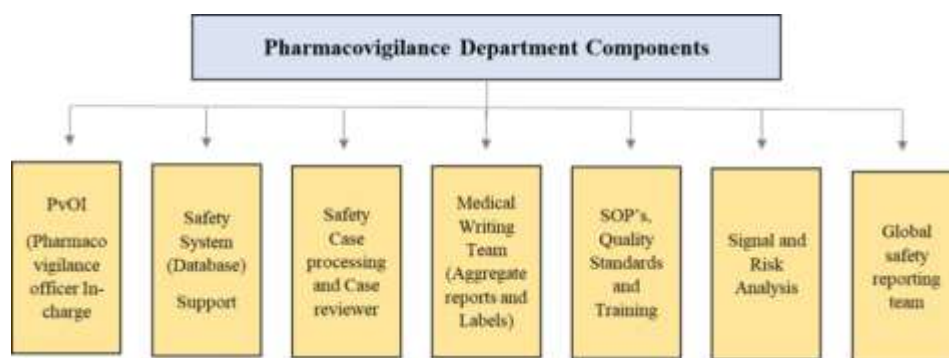


Figure no.5 Components of PV [28]

Passive Surveillance

Passive observation is when you don't create an aggressive company to control negative outcomes except for healthcare workers and other promotions to report safety. Fear- this is based on their initiatives and motivation for information.

A. Voluntary relationships:

Voluntary reporting allows healthcare workers or patients to freely notify the company, regulator, or group of unwanted effects on drugs without participating Search or collect planning data. In a

voluntary report, the physician, or patient shares observations regarding the response to the drug to the company or organization.

B. Systematic methods for evaluating voluntary reports:

Recently, people have experienced novel approaches to disclosing relationship security issues. However, many of these methods are still. The development and evaluation process determines the effectiveness of identifying security signals [29].

Active Surveillance

Sentinel Site: Provide and provide positive observations by the selected awning medical records and patient maintenance and/or the physician. Accurate data regarding the side effects communicated. Sites that have been carefully chosen are unable to give patients access to information like patient-specific data. a consensual structure of passive relationships. Additionally, this foot sent site may be used to gather specific data about drug usage, including misuse.

Pregnancy Monitoring for Drug Events: For active pharmacy supervision, monitoring of drug events involves detection of patients using electronic data via prescription or automated health Insurance complaints.

In the register: The register focuses on diseases such as drugs and specific effects and constitutes a patient list that separates common characteristics. These registers etc. In case of blood abnormalities, severe skin reactions, or congenital malformations, we will collect a complete set of information thank you Profiles in a promising way [30].

Spontaneous reporting

It is an accepted solar system and is often called "Spontaneous" report. Voluntary reporting depends on journalists Educated and motivated to record and present your observations. All actual healthcare professionals must conduct training; In the perception that community members point to unwanted influences, they point to culture from a perspective. Subsequent training should be conducted to accept the way to overcome Voluntary relationships, particularly underestimated limitations Report. This system presents its own advantages to support Unlike clinical trials, authentic clinical practice The

population is excluded. The duration of treatment is also limited. However, this system has many drawbacks, such as underestimation. As it is the mail, only the molecules are provided. Just like absence Information about the populations to which the medication is to be administered. So, it is difficult Determine accurately the risks associated with the suspect. moreover, Registered cases also have messages about bias. Other restrictions Include differences between quality of detail and missing details information. Despite all these drawbacks, the relationship is always spontaneous Cornerstone PV, because it allows you to request detection of Security warnings linked to drug use thanks to early detection of new one's Low frequency ADR [29,30].

Cohort Event monitoring

Monitoring cohort events (CEM) are primarily active forms of photoelectric systems Designed for specific targeted drugs for future observational research Undesired phenomena found on a particular drug. CEM Program First of all, you need to study another medication in your daily life. In addition, clinical practice is not useful in the initial stages of IV. It is a clinical trial, but it can also be useful when identifying related risks Drugs sold. It depends on New Zealand standards Intensive drug surveillance programme and UK recipes Support only in most countries for event monitoring. So, CEM is an early warning system that records a group of clinical patients' Specific treatment-related events to capture all related clinical events interesting drugs used in public health programs (PHP). Accurate Patients should be evaluated before treatment begins After treatment begins. This describes the events related to the above events Is the drug the cause of the drug event. CEM contains a record of all events, including the following data: Any New medical events (changes in medical aspects, strange



symptoms) (either diagnostic or laboratory research changes) Observation at a specific time before treatment begins It was recorded again. Subsequent observations must be taken after a specific temporary interval Clinical studies considering unknown side effects observed after treatment cohort initiation [31].

Pharmacovigilance Programme of India (Pvpi)

Structure of NCC

In the National Pharmacovigilance Programme of India, the NCC plays a significant role in collecting, analysing, and disseminating information regarding ADRs reported throughout the country. It has several essential functions that must operate smoothly, including data collection, processing, and analysis. Adverse event reports are submitted electronically from across India to the

NCC. These reports include details about patient information, specific drug information, and suspected ADRs, which are verified by NCC staff. They are responsible for analysing the data to identify trends and safety signals and determining if further investigation is necessary. Additionally, the NCC is tasked with sharing critical information with stakeholders, including regulatory authorities, to facilitate discussions on regulatory decisions concerning drug safety. Healthcare professionals should promote awareness of potential adverse drug reactions. The publication of reports on ADR trends in India should be prioritized. The NCC is situated within the Indian Pharmacopoeia Commission in Ghaziabad, Uttar Pradesh. Personnel working at the NCC are highly qualified professionals with expertise in pharmacovigilance, pharmaceuticals, and data analysis [32].

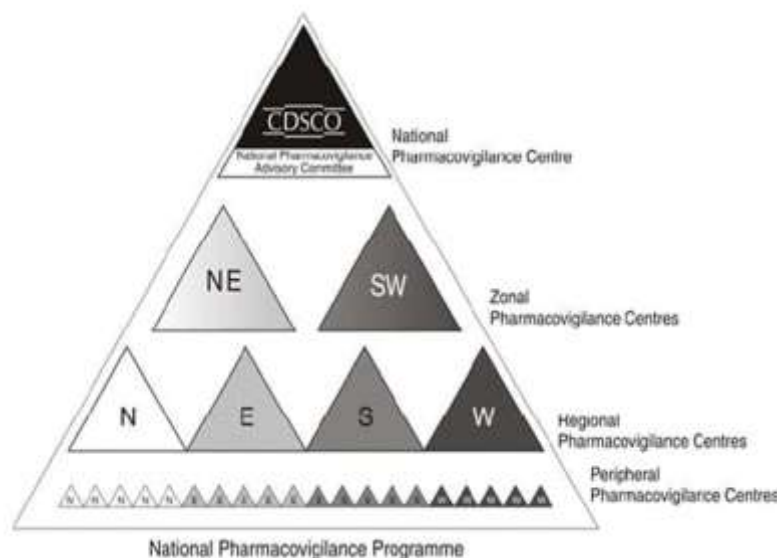


Figure no.6 NCC-Pharmacovigilance program of India [32]

Adverse Monitoring Centre (AMCs)

The National Coordinating Center (NCC) developed the Adverse Drug Reaction Monitoring Centers (AMCs) to collect adverse drug reactions (ADRs) from patients. Finding adverse medication responses that were missed in earlier clinical trial

operations is the main goal. The NCC gives the AMCs power and logistical support to enable the monitoring of these adverse medication reactions. At the moment, a sizable number of AMCs are in operation across the nation and are connected to India's Central Drugs Standard Control Organization (CDSCO). The CDSCO provides

standardized procedures for ADR reporting, risk management, and signal detection across various regulatory authorities. Moreover, the Council for International Organizations of Medical Sciences (CIOMS) works in partnership with the WHO and other relevant parties to develop pharmacovigilance methodologies and guidance, thereby enhancing global uniformity in drug safety monitoring [36].

Safety Specification in Risk Management

Non-Clinical data analysis

Non-clinical safety discoveries that clinical evidence has not sufficiently addressed, like:

1. This portion of the specification must define toxicity, which includes repeat-dose toxicity, reproductive/ developmental toxicity, nephrotoxicity, hepatotoxicity, genotoxicity, carcinogenicity, etc.
2. General pharmacology (nervous system, cardiovascular, including QT interval prolongation, etc.).
3. Interactions of drugs.
4. Additional data or information on toxicity.
5. It is crucial to take into account any criteria for non-clinical data if the product is meant to be used by specific populations.

Clinical data analysis

Limitations of the Human Safety Database

The limitations of the safety database (for instance, concerning the size of the study population and the criteria for inclusion/exclusion in the study) should be taken into account, and the consequences of these limitations regarding the prediction of the product's safety in the market should be clearly articulated. Special attention should be given to populations that are likely to be exposed during the

intended or anticipated use of the product in medical practice.

The global experience should be succinctly addressed, encompassing:

1. The degree of global exposure.
2. Any newly identified or distinct safety concerns.
3. Any regulatory measures pertaining to safety.

Populations Excluded from the Pre-Approval Phase

During the pre-approval stage, the specification must specify which populations have not been studied or have only had limited research done on them. This should have a demonstrable impact on the capacity to predict the product's safety in the market (CTD 2.5.5).

1. Children are among the populations that should be taken into consideration; however, they are not the only ones.
2. The older.
3. A pregnant or nursing woman.
4. Individuals with pertinent co-morbidities, such as renal or liver conditions.
5. Individuals whose illness severity deviates from what was shown in clinical studies.
6. Subpopulations having relevant and recognized genetic differences.
7. Individuals from different racial and/or cultural backgrounds [36].

Drug-Drug and Food-drug Interaction

It is essential to always consider the possibility of drug-drug interactions, considering the known aspects of the drug's metabolism, its mechanism of action, and the concurrent therapies. Depending on the circumstances, it may be adequate to evaluate adverse events in relation to concomitant therapy within the proposed pivotal clinical trials;



alternatively, it may be necessary to perform targeted studies. Several issues persist, including the predictability of *in vitro* studies, the applicability of interaction studies conducted on healthy volunteers to actual patients, and potential pharmacodynamic interactions that may not be anticipated by traditional pharmacology studies. Additionally, food-drug interactions can also be significant (for instance, the impact of grapefruit juice on the kinetics of various drugs); it is advisable to gather available information regarding experiences with products belonging to the same or similar chemical and pharmacological classes [37].

Post-marketing Surveillance

The term "post-marketing surveillance" (PMS) describes the methodical, ongoing observation of pharmaceutical goods following their approval and introduction to the market [38]. It includes gathering, examining, and interpreting information concerning the effectiveness and safety of drugs in practical contexts. Post-marketing monitoring is a continuous procedure that attempts to identify, evaluate, and avoid adverse effects or any other problems associated with drugs that may arise after a product has entered the market, in contrast to pre-market clinical studies, which offer insightful information during the drug development phase [39]. PMS serves as a watchful guardian, closely examining how well drugs work in a range of patient demographics and bringing to light potential advantages or hazards that might not have been apparent during pre-market analyses [40]. Due to PMS, 4% of new drugs were taken off the market because of safety issues, and nearly 20% of them received a black box warning after marketing [41].

CONCLUSION

Pharmacovigilance is essential for guarding the health of the public because it guarantees the effectiveness, safety, and quality of medications at every stage of their life cycle. By closely observing adverse drug reactions (ADRs) and the problems associated with drugs once a product is put on the market, it goes beyond pre-marketing clinical trials. Stronger patient safety, more informed regulatory decisions, more sensible drug use, and more confidence in healthcare systems are all benefits of effective pharmacovigilance. Given the increasing complexity of treatments and the widespread distribution of drugs, pharmacovigilance is still crucial for risk early identification, prompt management, and the global advancement of safer therapeutic practices.

REFERENCES

1. Wasiullah, M., Yadav, P., Vishwakarm, M., & Patel, D. K. (2025). *International Journal of Pharmaceutical Research and Applications*, 10(2), 2370–2376. Retrieved from <https://www.ijprajournal.com>
2. Mishra, M. K. (n.d.). *Indian Biological Sciences and Research Institute (IBRI)*, Noida.
3. Londhe, V. P., Chanshetti, R., & Dhole, S. N. (2024). *Pharmacovigilance: Past, present and future*. *Asian Journal of Pharmaceutical Research*, 14(2), 175–182. <https://doi.org/10.52711/2231-5691.2024.00029>
4. Jones, J. K., & Kingery, E. (2014). *History of pharmacovigilance*. In E. B. Andrews & N. Moore (Eds.), *Mann's pharmacovigilance* (3rd ed., pp. 11–24). John Wiley & Sons, Ltd.
5. Ridings, J. E. (Year unknown). *The thalidomide disaster: Lessons from the past*. In P. C. Barrow (Ed.), *Teratogenicity testing: Methods and protocols* (Methods in



- Molecular Biology, Vol. 947, pp. 575–586). Humana Press.
6. Fintel, B., Samaras, A. T., & Caria, E. (n.d.). The thalidomide tragedy: Lessons for drug safety and regulation. Retrieved from <http://helix.northwestern.edu/article/thalidomide-tragedy-lessons-drug-safety-and-regulation>
 7. World Health Organization. (2020). Pharmacovigilance: Ensuring the safe use of medicines. World Health Organization. <https://www.who.int/teams/regulation-prequalification/pharmacovigilance>
 8. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). (2023). ICH guidelines: Quality, safety, efficacy and multidisciplinary guidelines. ICH. <https://www.ich.org/page/ich-guidelines>
 9. Korade P B, Khaire R D, Kathale A A, Sanke L D, Bhandare T S, Ghuge S K, Pharmacovigilance: A Pillar of Modern Drug Safety , *Asian Journal of Pharmaceutical Research and Development*. 2025; 13(5):60-68, DOI: <http://dx.doi.org/10.22270/ajprd.v13i5.1626>
 10. World Health Organization. (2021). WHO Global Benchmarking Tool (GBT) for evaluation of national regulatory systems: Revision VI. World Health Organization. <https://www.who.int/publications/i/item/WHO-MHP-RPQ-GBT-2021>
 11. S., Raut, N., Ban, G., Urgunde, J., Biradar, V., Shindalkar, S., Wable, H., Chavan, S., & Bobade, V. (2025). An overview of clinical trial review processes in India: Roles and responsibilities of regulatory bodies. *International Journal of Pharmaceutical Sciences*, 3(5), 329–339. <https://doi.org/10.5281/zenodo.15333182>
 12. Chidambaram, A. G., & Josephson, M. (2019). Clinical research study designs: The essentials. *Pediatric Investigation*, 3(4), 245–252. <https://doi.org/10.1002/ped4.12159>
 13. Sharma, S., Sharma, K., Verma, P., Rahi, S., & Rana, A. (2022, June 15). Comparative analysis of new drugs and clinical trial rules 2019 and its impact on approval process of oncology drugs. *International Journal of Drug Regulatory Affairs*, 10(2), 112–130. Retrieved from <http://ijdra.com/index.php/journal/article/view/543>
 14. StoryMD. (n.d.). Interventional study – Types of clinical trials. Retrieved October 15, 2025, from <https://storymd.com/asset/Qd934pUgAg-interventional-study-types-of-clinical-trials?newsletter=show>
 15. Central Drugs Standard Control Organisation (CDSCO). (n.d.). About CDSCO: Functions and responsibilities. Ministry of Health & Family Welfare, Government of India. Retrieved [insert date you accessed it, e.g., October 16, 2025], from <https://cdsco.gov.in>
 16. U.S. Food and Drug Administration (FDA). (n.d.). Investigational new drug (IND) application. U.S. Department of Health and Human Services. Retrieved [insert access date, e.g., October 17, 2025], from <https://www.fda.gov>
 17. Yadav, H. P. K. (2023). A review article on Investigational New Drug (IND) applications: types, procedures and regulatory aspects. *GSAR Journal of Medical Sciences*, Retrieved from <https://gsarpublishers.com/wp-content/uploads/2023/02/GSARJMS052023-Gelary-script.pdf>
 18. Comparison of Drug Approval Process in United States & Europe – Scientific Figure on Research Gate. Available from: <https://www.researchgate.net/figure/nvestigational-New-Drug->



- Application_fig2_263657519 [accessed 17 Oct 2025]
19. Dhulia, I., Patel, H., Chauhan, N., & Pardeshi, N. (2021). FDA's drug regulatory pathways, its development strategies and regulatory considerations. *International Journal of Drug Regulatory Affairs*, 9(2), 6-15. <https://doi.org/10.22270/ijdra.v9i2.460>
 20. Rawat, S., & Gupta, A. (2011). Regulatory requirements for drug development and approval in United States: A review. *Asian Journal of Pharmaceutical Research*, 1(1), 1-6.
 21. Kumar, R., & Singh, J. (2017). An overview of regulatory requirements for drug approval: Generic drugs and the Hatch-Waxman Act. *International Journal of Pharmaceutical Sciences Review and Research*, 44(1), 28-34.
 22. Dharani, Thummala & Kumar, Pachala & Phanindra, Desaboyina & Nagabhushanam, M & Bonthagarala, Brahmaiah & Ramakrishna, G & Sindhu, Y & Kumar, Santosh. (2022). A REVIEW ON ABBREVIATED NEW DRUG APPLICATION (ANDA). [10.20959/wjpps20225-21944](https://doi.org/10.20959/wjpps20225-21944).
 23. Central Drugs Standard Control Organization (CDSCO). (2019, March). New Drugs and Clinical Trial Rules, 2019 (GSR 227[E]). CDSCO. Retrieved March 10, 2022, from https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdfdocuments/
 24. S. Lahiry. (2020). New drug and clinical trial rules, 2019 – What academicians need to know. *Indian Journal of Dermatology, Venereology & Leprology*, 86(2), 103-110. https://doi.org/10.4103/ijdv1.IJDVL_328_19
 25. Cimino, J., & Braun, C. (2023). Design a Clinical Research Protocol: Influence of Real-World Setting. *Healthcare (Basel, Switzerland)*, 11(16), 2254. <https://doi.org/10.3390/healthcare11162254>
 26. Pinto, R. Z., & Ferreira, M. L. (2023). Design a clinical research protocol: Influence of real-world setting and regulatory expectations. *Healthcare*, 11(16), 2254. <https://doi.org/10.3390/healthcare11162254>
 27. Issues, challenges, and the way forward in conducting clinical trials among neonates: investigators' perspective – Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Process-of-regulatory-approval-for-clinical-trials-in-India_fig1_335630743 [accessed 18 Oct 2025]
 28. World Health Organization. (2024). Pharmacovigilance: Ensuring the safe use of medicines—A review of global practices. *WHO Drug Information*, 38(1), 5-18. <https://www.who.int/publications/i/item/pharmacovigilance-ensuring-safe-use-2024>
 29. Schematic diagram of complete pharmacovigilance system components [Scientific figure]. (n.d.). ResearchGate. Retrieved October 10, 2025, from https://www.researchgate.net/figure/Schematic-diagram-of-complete-Pharmacovigilance-system-components_fig1_352152535
 30. Thota, P., Thota, A., Sarma, P., & Medhi, B. (2022). An overview of spontaneous reporting, targeted spontaneous reporting and cohort event monitoring – pharmacovigilance methods: Myths and facts. *Journal of Pharmacy Practice & Community Medicine*, 8(1), 8-13. <https://doi.org/10.5530/jppcm.2022.1.3>
 31. Bortoli, A., & McCarthy, M. (2024). A comparison of active pharmacovigilance strategies used to monitor adverse events to antiviral agents: A systematic review. *Drug Safety*, 47 (8), 1203-1224. <https://doi.org/10.1007/s40264-024-01470-0>
 32. Cohort event monitoring: A practical method for active pharmacovigilance in resource-



- limited settings. *Drug Safety*, 42(12), 1493–1506. <https://doi.org/10.1007/s40264-019-00862-9>
33. A new era of drug safety – New EU pharmacovigilance (PV) legislation and comparison of PV in EU, US and India – Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/National-Pharmacovigilance-Program-NPP-of-India-21_fig1_290056515 [accessed 16 Oct 2025]
34. Kalaiselvan, V., Thota, P., & Singh, G. N. (2019). Pharmacovigilance Programme of India: Recent developments and future perspectives. *Indian Journal of Pharmacology*, 51(6), 373–378. https://doi.org/10.4103/ijp.IJP_821_18
35. Nimesh S, Ashwlayan VD (2018) Pharmacovigilance: An Overview. *Int J Pharmacovigil* 3(1):1-6.
36. System of adverse drug reactions reporting: What, where, how, and whom to report? – Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Suspected-adverse-drug-reaction-reporting-form_fig1_282895881 [accessed 15 Oct 2025]
37. The ICH E2E pharmacovigilance planning guideline. *Drug Safety*, 28(10), 957–970. <https://doi.org/10.2165/00002018-200528100-00006>
38. Drug–drug interactions: Predictability, clinical relevance, and regulatory aspects. *Drug Metabolism and Disposition*, 47(12), 1331–1346. <https://doi.org/10.1124/dmd.119.087338>
39. Alomar, M., Tawfiq, A. M., Hassan, N., & Palaian, S. (2020). Post marketing surveillance of suspected adverse drug reactions through spontaneous reporting: current status, challenges and the future. *Therapeutic advances in drug safety*, 11, 2042098620938595. <https://doi.org/10.1177/2042098620938595>
40. Zhang X, Zhang Y, Ye X, et al. Overview of phase IV clinical trials for postmarket drug safety surveillance: a status report from the ClinicalTrials.gov registry. *BMJ Open* 2016; 6: e010643.
41. Alomar, M., Tawfiq, A. M., Hassan, N., & Palaian, S. (2020). Post marketing surveillance of suspected adverse drug reactions through spontaneous reporting: current status, challenges and the future. *Therapeutic advances in drug safety*, 11, 2042098620938595. <https://doi.org/10.1177/2042098620938595>

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