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CONCEPT OF PHARMACOVIGLANCE

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ABSTRACT

Pharmacovigilance is defined as 'the activities involved in the detection, assessment, understanding, and prevention of adverse effects or any other drug related problems.' All drugs have the Knowledge of these principles is fundamental to making informed treatment decisions and to aid in the discussion of risk with patients. he capacity to cause adverse effects and no drug is completely safe Technology and financial challenges hinder Pv incorporated into the healthcare systems of developing countries. In a developing healthcare system, in addition to its inherent deficiencies, practitioners are afraid to use Pv, which is indicated as evidence of its flaws.

KEYWORDS: All drugs have the Knowledge of these principles is fundamental to making informed treatment decisions and to aid in the discussion of risk with patients.

INTRODUCTION

Consuming a drug is equivalent to consume a risk. It is only when the benefit associated with the drugs are more than the risk, that the consumption of a drug is justified. Thus, it is benefit versus risk ratio of the drug which decides whether a drug is to be taken or not. The next question is how to measure risks and how to measure the benefits. Due to individualization of drugs to patients, it is the clinical judgment of the physician to identify what will benefit the patient. At the same time, risk associated with the drug can be ascertained by observations related to pharmacovigilance. The studies related to pharmacovigilance indicate what are the possible risks associated with the drug. Even drug can be associated with possible adverse reactions, intended or unintended. The only exception to this generality is the case of drug whichis given in case of deficiency of specific components like vitamins or minerals. It is the study of possible adverse reactions of drugs which constitutes the essential content of Pharmacovigilance. This takes us to the definition of Pharmacovigilance.

Pharmacovigilance is the science and activities related to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems. Spontaneous reporting of adverse events and adverse drug reactions is the commonest methodutilized for generating safety data.

Definition for Pharmacovigilance

Pharmacovigilance is defined as “the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, principally long term and short term adverse effects of medicine."

Scope and Objectives of Pharmacovigilance

- To reduce the frequency and severity of adverse effect of drug and improving their safety and efficacy.
- To develop an effective ADR (Adverse Drug Reactions) reporting channel, such as the online reporting system.
- To educate all the parties to participate actively in the pharmacovigilance reporting system.
- To encourage the safe, rational and more effective use of medicines.
- Increase the awareness of healthcare professionals and the public on the understanding of the importance of pharmacovigilance.
- To Improve communication for adverse drug reaction between stakeholders, the health careproviders, manufacturer and regulators for pharmacovigilance.
- To emerge as a National Centre of Excellence for Pharmacovigilance activities.
- To create a nation-wide system for patient safety reporting.
- To identify and analyse new signal from the reported cases.
- To analyse the benefit - risk ratio of marketed medications.
- To generate evidence based information on safety of medicines.
- To support regulatory agencies in the decision-making process on use of medications.
- To communicate the safety information on use of medicines to various stakeholders to minimise the risk.
- To emerge as a national centre of excellence for pharmacovigilance activities.
- To collaborate with other national centres for the exchange of information and data management.
- To provide training and consultancy support to other national pharmacovigilance

centres across globe.

- To promote rational use of medicine.

Scope of Pharmacovigilance can be summarized in the following key areas

Adverse Event Reporting: One of the primary responsibilities of pharmacovigilance is the collection and analysis of adverse event reports. Healthcare professionals, patients, and pharmaceutical companies submit these reports when they suspect that a medication may havecaused harm or an unexpected reaction. These reports are crucial for identifying potential safetyissues.

Signal Detection: Pharmacovigilance experts use statistical and analytical tools to detect signals, which are patterns or trends in adverse event reports that may indicate a previously unrecognized safety concern. Identifying signals helps prioritize further investigations.

Risk Assessment: Once a potential safety concern is identified, pharmacovigilance professionals conduct in-depth assessments to determine the risk-benefit profile of a medication. This involvesevaluating the severity of adverse events and weighing them against the therapeutic benefits ofthe drug.

Post-Marketing Surveillance: Medications undergo rigorous testing in clinical trials before they are approved for use. However, pharmacovigilance continues after a drug's approval, monitoringits safety in real-world settings. This is vital because some adverse events may be rare or occur only after long-term use.

Classification of Pharmacovigilance Methods

1. **Passive Pharmacovigilance**

A. Spontaneous Report

B. Case Series

2. **Stimulated Reporting**
3. **Active Surveillance**

A. Sentinel Sites

B. Drug event monitoring

C. Registries

4. Comparative Observational Studies

A. Cross-sectional study (survey)

B. Case control study C. Cohort study

5. Targeted clinical investigation

A. PK and PD studies

B. Genetic testing

C. In special popolatin

D. Large simpified trial

6. Descriptive studies

A. Natural history of studies

B. Drug utilization study

History

Pharmacovigilance in India was initiated way back in 1986 with a formal adverse drug reaction (ADR) monitoring system, under supervision of the drug controller of India Later, the National Programme of Pharmacovigilance was launched in 2005, and was renamed as the Pharmacovigilance Programme of India (PvPI) in 2010. The Pharmacovigilance Programme of India (PvPI) was started by the Government of India on 14th July 2010 with the All India Institute of Medical Sciences (AIIMS), New Delhi as the National Coordination Centre for monitoring Adverse Drug Reactions (ADRs) in the country for safeguarding Public Health.

Many developed countries set up their pharmacovigilance programs following the Thalidomide scandal in the 1960s. India set up its program in the 1980s. This general concept of drug safety monitoring went through different forms, but the Central Drugs Standard Control Organisation established the present Pharmacovigilance Program of India in 2010. Now the program is well integrated with government legislation, a regulator as leader, and a research center as part of the Indian Pharmacopoeia Commission.

Mission: The mission of PvPI is to safeguard the health of the Indian population by ensuring that the benefit of use of medicine outweighs the risks associated with its use. Since there exist considerable social and economic consequences of adverse drug reactions and the positive benefit/cost ratio of implementing appropriate risk management - there is a need to engage healthcare professionals and the public at large, in a wellstructured programme to

build synergies for monitoring adverse drug reactions in the country**.**

Purpose: The purpose of the PvPI is to collate data, analyse it and use the inferences to recommend informed regulatory interventions, besides communicating risks to healthcare professionals and the public. The broadened patient safety scope of pharmacovigilance includes the detection of medicines of substandard quality as well as prescribing, dispensing and administration errors. Counterfeiting, antimicrobial resistance, and the need for real time surveillance in mass vaccinations are other pharmacovigilance challenges which need to be addressed**.**

Vision: The vision of PvPI is to improve patient safety and welfare in Indian population by monitoring drug safety and thereby reducing the risk associated with use of medicines. Ultimate safety decisions on medicines may need considerations of comparative benefit/risk evaluations between products for similar indications, so the complexity is great.

CONCLUSION

Current progress in pharmacovigilance is marked by increasing use of databases and by attempts to make the process more proactive and organized. Attempts are being made to augment the spontaneous, random nature of the generation of pharmacovigilance data and to make the process more systematic and struc-tured. These changes are emphasized by the recent guidance documents for industry by both EMEA and FDA on pharmacovigilance planning and risk management. This emphasis on planning a pharma-covigilance programme for a drug and trying thought-fully to minimize risk appears constructive and, to some of us, long overdue. It is notable that the empha-sis on proactive safety planning is linked with an expectation that the suspicions arising from sponta-neous reporting will rapidly be tested by formal phar-macoepidemiological studies conducted in organized and validated databases or prospective studies.

It is in everyone's interest to develop safe and effective medicines and provide access to patients for whom benefits will outweigh harms. Post-approval surprises, such as drug withdrawals, are not innocent of harm for the drug is precipitously denied to large numbers of patients who found it safe and effective. There has been a coming together of academic, regu-latory and industrial interests across many countries to produce the guidance documents mentioned above as well as good practice guidelines for the conduct of pharmacopepidemiology studies (International Soci- ety for Pharmacoepidemiology, 2004).

Pharmacvigilance Inspection

The safety of drugs is of paramount importance to patients and healthcare professionals. The pharmaceutical industry has an ethical and legal responsibility to ensure that the products they sell will not harm the patients they are intended for. The repercussions of a new drug having a potentially serious side-effect profile are enormous for patients, healthcare professionals and the industry.

There have been many drugs that were very successful and benefited thousands of patients, but were later found to have serious side-effects, resulting in their withdrawal. The most notable recent example was Vioxx, launched in 1999 and withdrawn in 2004 with total sales of $2.5 billion from 100 million prescriptions issued. The cost to Merck in terms of loss of revenue, personal injury lawsuits and reputation has been significant. There is also the impact on the class of drugs,with an increase in the level of testing required for all COX 2 inhibitors in development, and monitoring of safety when on the market.

The regulatory bodies that approve licenses have a responsibility to protect the public; in the mission statement of the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom, it states that their remit is to "enhance and safeguard the health of the public by ensuring that medicines work and are safe."

The US Food and Drug Administration (FDA) in the United States has been severely criticized for not acting on information regarding heart attacks and stroke from healthcare professionals prescribing Vioxx. As a result, the FDA has established an independent Drug Safety Oversight Board in 2005 to oversee the management of drug safety issues. In addition, it has issued guidance for industry on good pharmacovigilance practices and pharmacoepidemiologic assessment (March 2005).

The guidance includes the requirement for routine risk management and risk minimization activities to be conducted by the industry.

Statutory inspections may be notified to the MAH in advance (usually 1-3 months in Europe), or they may be given virtually no notice if there is a valid reason for a 'triggered' or 'for cause' inspection. The notification letter will include a request for documentation describing the pharmacovigilance quality system, both nationally and globally (if a global company). The MHRA requires sponsor companies to complete a specific document called the

'Summary of Pharmacovigilance Systems' or SPS.

Once the inspection team have reviewed all of the documents sent to them, they prepare an 'Inspection Plan', which is essentially an agenda indicating which functions will be interviewed and when. The company has an opportunity to comment on the Inspection Plan to ensure that they can get the right people in the right place at the right time. The Inspection Plan will include interviews with non-pharmacovigilance personnel such as Medical Affairs, Regulatory Affairs, Sales and Marketing and Clinical Operations. Companies must ensure that all affected personnel are aware of the inspection and make themselves available.

The number of inspectors and the duration of the inspection are dependent on the size of the company's product portfolio. The inspection team may consist of two inspectors spending 2 days at the company, or up to four inspectors for more than a week. Inspectors may want to conduct interviews in parallel to maximize the time available, so companies must be prepared to find appropriate facilities to accommodate the inspection interviews.

The overall percentage satisfaction rate was 90% (80-97%). Less than 2% of the scores were in the 'dissatisfied' category and none was in the 'totally dissatisfied' category. The dissatisfaction reported mainly concerned the completion of the SPS. The MHRA has considered that the format and use of the SPS may need to be reviewed.

Staff within the pharmacovigilance department must be trained, not just in the SOPs, but also on the regulations that apply to pharmacovigilance. This is to ensure that they understand their legal responsibilities and appreciate the significance of what they are doing. The QPPV must be very clear on their responsibilities, and these should also be documented in policies and procedures. Senior management should be seen to be providing the necessary support and resource to the QPPV to be able to perform their role in accordance with the legal requirements. Out-of-hours systems should be tested on a regular basis to ensure that the QPPV or delegate can be contacted. Ensure that all pharmacovigilance staff know when the QPPV is not available and who their deputy or delegate.

As discussed previously, the penalties for non-compliance can be quite severe. Most agencies allow companies to correct deficiencies and then re-inspect to confirm that appropriate corrective action has been taken. However, if the deficiencies are considered to be so serious that patients could be at risk, the authorities can suspend a license or CTA, which could have

a significant impact on the company's revenue and reputation. In the scheme of things, the cost of implementing and maintaining an effective pharmacovigilance quality system is insignificant in comparion.

Spontaneuos Report

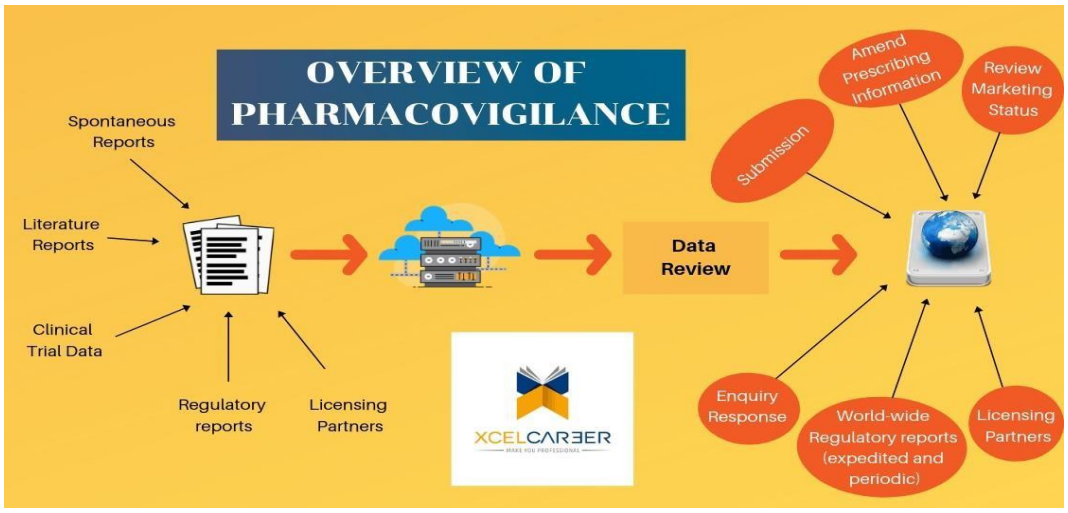


Fig. 1: Overview Of Pharmacovigilance.

When a physician suspects a serious clinical event to be an ADR, they are encouraged to completea questionnaire and notify the country's drug regulatory agency about the suspected ADR. An adverse event is serious when it results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.[3] In some countries, the spontaneous reporting scheme has been extended to reporting from pharmacists, nurses, and even patients.

Although the spontaneous reporting questionnaire differs from country to country, in general the information collected includes patient details (such as age, sex, weight), details on the suspected drug (such as dose, duration of treatment), details on the suspected reaction(s) (such as description of the event, seriousness, outcome), medical history of the patient, and other concomitant medication that the patient was taking. Examples of spontaneous reporting systems include the "Yellow card scheme" operated by the UK Medicines and Healthcare Products Regulatory Agency (MHRA) and the Commission on Human Medicines, and the Adverse Event Reporting System (AERS) which is a database of spontaneous reports received by the US Food and Drug Administration (FDA) through the MedWatch form. In India the suspected ADR reporting scheme is undertaken by the Central Drugs Standard

Control Organization (CDSCO).

The spontaneous reporting system is a passive surveillance method that solely relies on the healthcare professionals to detect and take the initiative to report an ADR. Reporting varies with the reporters' skill and experience to detect the ADR, their level of understanding of the spontaneous reporting system, and their workload.[7] Furthermore, ADR reporting is also influenced by other factors such as the media, published literature, and age of the drug. A higher number of reports are seen in the first two years after drug launch.

A survey conducted to assess doctors' attitudes toward reporting of ADRs in Netherlands showed that uncertain causality, the ADR being trivial, and the ADR being too well known were the most frequent reasons for not reporting. Other reasons for not reporting were lack of knowledge, for example, not knowing how to report, and lack of awareness of the existence of a reporting scheme. This survey also showed that general practitioners (GPs) were more likely to report an ADR than specialists (51% vs 35%).[8] Another study looking at reporting of ADRs by GPs showed that GPs who actively report ADRs had more knowledge on ADR reporting and were more interested in pharmacotherapy than their nonreporting colleagues.[9]

In an attempt to improve reporting of suspected ADRs, studies have been conducted to examine the impact of interventions on ADR reporting; one such study was undertaken in a large teaching hospital in Spain.[10] A multifaceted intervention approach to improving spontaneous ADR reporting was undertaken, and interventions included economic incentives, physician training and education (about spontaneous reporting/pharmacovigilance, selection of serious ADRs, etc.), providing feedback to physicians about signals identified by the pharmacovigilance program, and distribution of list of the most important ADRs to be reported. The result of the interventions was a quantitative and qualitative improvement of spontaneous reporting of ADRs by hospital physicians. Other studies analyzing the effects of educational interventions on spontaneous reporting of ADRs have also shown improvement in reporting as a result of these interventions.

Literature Report

Incorporating data from medical and scientific literature is a paramount aspect of patient safety. This wealth of knowledge often constitutes a substantial part of the safety profile of medicinal products. From providing insights on potential side effects to shedding light on

different patient experiences, this literature contributes significantly to how we understand and navigate the safety of medical products.

Regulatory bodies hold medicinal products' marketing authorization holders (MAHs) to a high standard. One key aspect of their responsibility is performing regular scientific literature searches, including unpublished manuscripts and abstracts presented at medical or scientific conferences.

To underscore the importance of literature monitoring in pharmacovigilance, consider that properly conducted searches can lead to important discoveries, timely interventions, and overall improved product safety. On the other hand, inadequate searches can result in missed opportunities, overlooked risks, and in some cases, significant patient harm.

Types of Literature Searches

Literature searches generally fall into two categories. First, **exhaustive searches** cast awide net across various databases and resources, capturing a broad spectrum ofavailable literature on a given subject. Second, **selective searches** focus on specific databases or key publications, often targeting high-impact literature.

Exhaustive searches

or systematic reviews, aim to include all available evidence on a specific research question. This involves extensive searching of several databases, websites, and sometimes even manual searching of journals and books to ensure no relevant study is overlooked.

The exhaustive search is labor-intensive and requires a clear understanding of the topic and complex search strategies. However, the end result is a comprehensive overview of the literature, including studies of all levels of quality and size. This approach is often used when performing meta-analyses, where the results of several studies are combinedto provide a more definitive answer to a research question.

Selective Searches

On the other hand, selective searches are more focused and usually target specific databases or key publications. Instead of casting a wide net, selective searches aim at catching 'big fish', which refers to high-impact literature that has the potential to change practices or policies.

This method requires knowledge about the topic and the ability to discern the importance of different pieces of literature. The targeted databases or journals often have high impact factors, meaning their published works are frequently cited in other research. While less comprehensive than exhaustive searches, selective searches are quicker and more feasible in certain circumstances, especially when time is limited.

The choice between the two depends on the research question, the project's scope, and the available resources.

Global vs. Local Literature Searches

When conducting research, you might come across the terms 'global literature search' and 'local literature search.' Understanding the differences between these two methods can significantly influence the depth and breadth of the findings of a research project. Let's dive into the characteristics that distinguish global and local literature searches.

Global Literature Searches

Global literature searches are broad and comprehensive. They seek to capture the full scope of existing research on a topic, regardless of the geographical origin of the data or the research institution. Global searches often employ multiple databases and resources, not limited to any specific country or region.

A global literature search intends to gather information from diverse sources, giving researchers an extensive understanding of the subject matter. This approach offers several benefits, including a broad perspective on the topic, a wide range of data, and the inclusion of different cultural, geographical, and socioeconomic contexts. However, it may require more time and resources due to the vast amount of information that needs to be reviewed and analyzed.

Clinical Trials

Pharmacovigilance (PV) for clinical trials (CT) is the duty and responsibility of the sponsor and investigator to ensure a continuous surveillance of the benefit: risk-relationship of the interventional exposure of the trial participants to investigational medicinal products and to inform the competent authorities, ethics committees and investigators of any relevant unfavourable change of this relationship as might become apparent in consequence of the trial.

In the EU, the European Economic Area (EEA) and the EU Member States (MS), PV of investigational medicinal products (IMP) and non-investigational products (NIMP) in CTs irrespective of their regulatory status (authorised or not) is an inherent albeit subordinate aspectof good clinical practice (GCP). Therefore PV of CTs is subject to the international and national regulations on the orderly conduct of CTs and GCP compliance.

Although relying on the process resources put in place by the sponsor for Eudravigilance reporting, PV of CTs requires its own GCP-compliant trial specific provisions, including risk-based PV-quality management, review of the safety reference information in the investigator brochure, review of the PV-information and instructions in the CT protocol, investigator training and instruction, on-study capture and analysis of safety signals, expert review of serious adverse events (SAE), and expedited handling of SAE and serious unexpected serious adverse reaction (SUSAR) reports.

PROCESS OF CLINICAL TRIALS

- Step 1: Discovery and development
- Step 2 : preclinical Research
- Step 3: clinical research
- Step 4: FDA Drug review
- Step 5: FDA Drug marketing drug safety monitoring

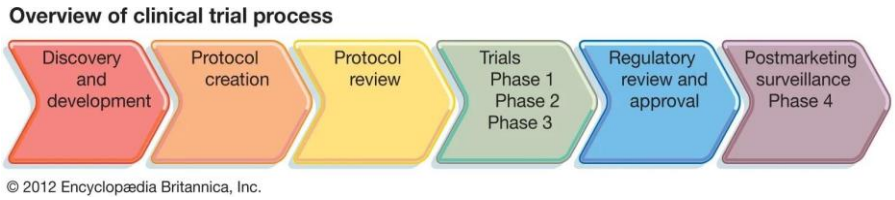


Fig. 2: Overview of Clinical Trial Process.

PROTOCOL DESIGNING CLINICAL TRIAL

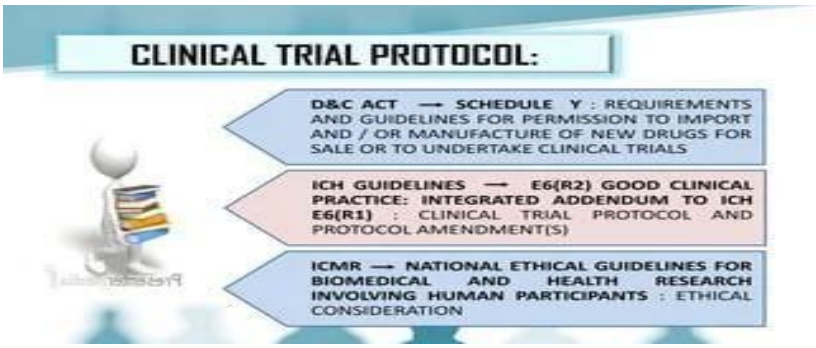


Fig. 3: Clinical Trial Protocol.

Process of clinical trials

It is a systematic investigation in human subjects for evaluating the safety & efficacy of any new drug. Clinical trials are a set of tests in medical research and drug development that generate safety and efficacy data for health interventions in human beings. • Clinical trials are conducted only when satisfactory information has been gathered on the quality of the nonclinical safety health authority/ethics committee approval is granted in the country where approval of the drugis sought. • Clinical Trial is the mainstay for bringing out New Drugs to the Market.

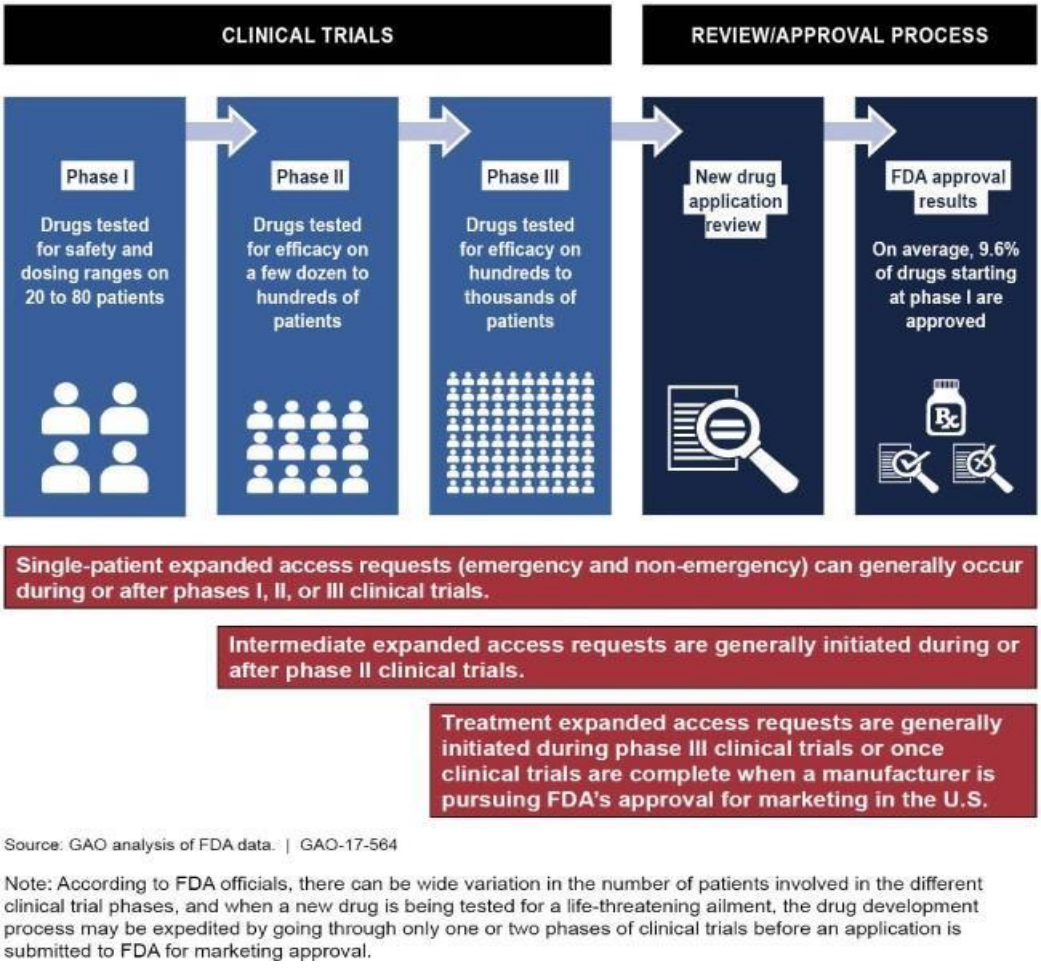


Fig. 4: phases of clinical trial.

Central drug standard control organization (CDSCO)

The CDSCO of India is main regulatory body for regulation of pharmaceutical, medical devices and Clinical Trials. Head office of CDSCO is located in NEW DELHI and functioning under the control of Directorate General of Health Services, ministry of health and family welfare Government of india.

Licensing Partner

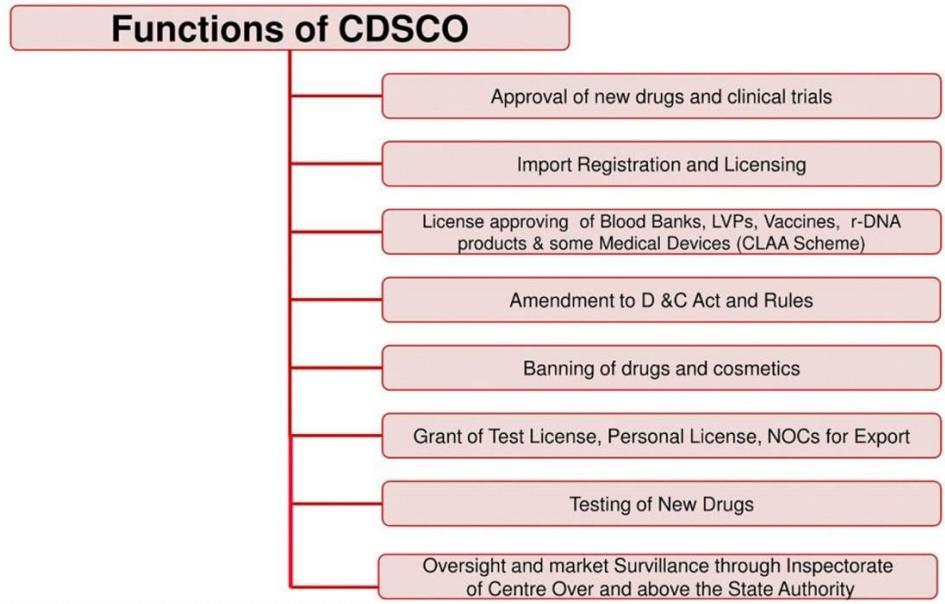


Fig. 5: function of CDSCO.

Basic legal principles everybody knows, but not everybody applies

- PhV obligations are the legal responsibility of the MAH.
- If you are the MAH and things go wrong, for regulatory purposes, it is irrelevant that the problemswere due to the actions or failures of a 3rd party working for the company or on its behalf.
- Licensing arrangements – one company who holds IP rights authorises another to use them inconnection with activities related to a products or products.
- Outsourcing arrangements – MAH buys a service from a separate entity/person (eg company ornatural person).

"Management" of licensing and outsourcing relationships involves steps taken

- *ƒ* Before the contract is signed *ƒ* Whilst the contract is in place.
- To provide for a period after the arrangement is over.

Therefore

- Choose partners and contractors with care
- Perform adequate due dilligence before entering the contract
- Ensure that the structure of the arrangements is optimal
- Address the impact of the regulatory requirements on the way a marketing deal/service contract is structured early on

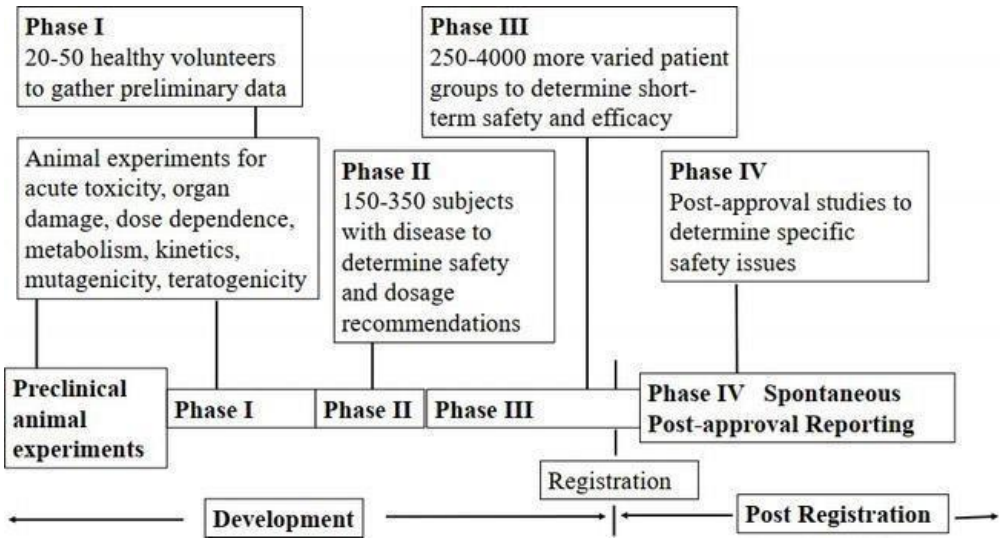
- Provide checklists for negotiators
- Have a contract dealing comprehensively with PhV issues*
- Actively manage the relationship: are the parties performing their obligations? How do you know?
- Reserve the right to audit and implement monitoring processes
- Have a process for addressing problems arising

Protection afforded by a contract : satisfying the regulators

- MAH to provide information of "such arrangements" to CA
- Contractors to implement QA and QC and must accept being audited.
- Co-marketers to avoid duplicate reporting to Eudravigilance
- Part I section 2 deals with the requirements for systems. Section 2.2 requires updates, product-specific addenda for productspecific arrangements arising in licensing situations, documentation, quality management systems

ADR (Adverse Drug Reaction)

The discovery of a new drug can usually take 10-15 years. Within this time period, the candidate drug is screened for its beneficial as well as for its side effects. But the side, adverse or toxic effects cannot be detected to a full scale due to some special reasons.



Types of Adverse drug reaction

Type A: Augmented pharmacologic effects - dose dependent and predictable Intolerance side effects.

Type B: Bizarre effects (or idiosyncratic) - dose independent and unpredictable.

Type C: Chronic effects

Type D: Delayed effects

Type E: End-of-treatment effects TypeF: Failure of therapy

Type A Augmented (dose related)

- Related to exaggerated pharmacological effects of drug
- E.g. hyperglycaemia with insulin, hypotension by beta blockers, NASAID`s induced gastric ulcers.

Type B Bizarre (Idiosyncratic)

- Unexpected, unpredictable, related to patient factors like genetic predisposition.
- E.g. Penicillin hypersensitivity, malignant hyperthermia.

Type C Chronic

- Uncommon, irreversible, unexpected, unpredictable.
- Due to long term use of drugs.
- E.g. Hypothalamic pituitary adrenal axis suppression by corticosteroids.

Type D Delayed

- Time related
- E.g. Teratogensis, carcinogenic like clear cell cancer of female reproductive tract

Type E End of Treatment

- Occurs due to sudden discontinuation of the drug after long term therapy.
- E.g. Adrenocortical insufficiency due to sudden withdrawal of corticosteroids, MI due to beta blockers withdrawal.

Type F Failure of Therapy

- Common, dose related
- Often caused by drug interactions
- E.g. Inadequate dosage of oral contraceptive particularly when used with specific enzyme

Severity of Adverse Drug Reactions

Adverse effects are any unwanted effects of a drug. There is no universal scale for describing or measuring the severity of an adverse drug reaction. Assessment is largely subjective. Reactions can be described as.

- Mild
- Moderate
- Severe
- Lethal (deadly)

➢ **Mild adverse drug reactions**

Mild reactions usually described as of minor significance include

- Digestive disturbances (such as nausea, constipation, diarrhea)
- Headaches
- Fatigue
- Vague muscle aches

➢ **Moderate adverse drug reactions**

Moderate reactions include

- Rashes (especially if they are extensive and persistent)
- Visual disturbances (especially in people who wear corrective lenses)
- Muscle tremor
- Difficulty with urination (a common effect of many drugs in older men)

Severe adverse drug reactions: Severe reactions include those that may be life threatening (such as liver failure, abnormal heart rhythms, certain types of allergic reactions), those that result in persistent or significant disability or hospitalization, and those that cause birth defects. Severe reactions are relatively rare. People who develop a severe reaction usually must stop using the drug and must be treated. However, doctors must sometimes continue giving high-risk drugs (for example, chemotherapy to people with cancer or immunosuppressants to people undergoing organ transplantation). Doctors use every possible means to control a severe adverse drug reaction.

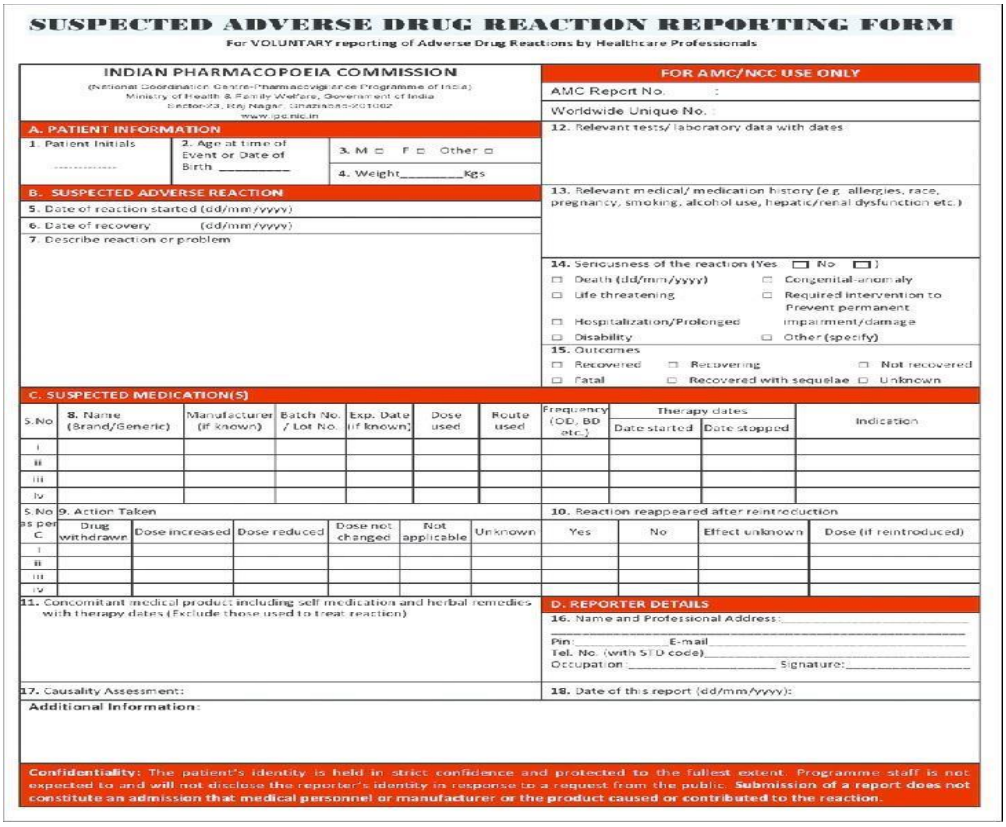
Lethal adverse drug reactions: Lethal reactions are those in which a drug reaction directly or indirectly caused death. These reactions are typically severe reactions that were not detected in time or did not respond to treatment. Lethal reactions can be the reasons that some drugs are withdrawn from the market (such as troglitazone and terfenadine).

List of national adverse drug monitoring center

Table No. 1.

ADRs Monitoring Centres	*function*
NCC- PvPI IPC –Ghaziabad, Up	1.Monitoring and reporting of ADR 2.Conduct training workshops and CME 3.Publication of Medicines safety newslette
Zonal/Sub zonal CDSCO Officers	Provide administrative support to ADRmonitoring officers
CDSCO HQ, NEW DELHI	Take appropriate regulatory decision and actions on the basis of recommendation ofPvPI
Department of Pharmacology, AIIMS, Delh	This department mainly focus on in the areaof molecular pharmacology, inflammatory research, after market studies.
Institute of Pharmacology, Chennai	To deal with different ADR which comes under the Pharmacovigilance program ofINDIA
AIIMS, Bhatinda	ADR monitoring centre actively collecting ADR from various clinical department as Punjab have highest number of patients inINDIA
Department of Pharmacology, Medical College, Guwahati, Assam	To generate evidence based information onsafety of medicines and study ADR
Department of Pharmacology, JIPMER, Pondicherry	Monitoring of Adverse drug reactions under pharmacovigilance program of India
AIIMS, Nagpur	The vision is to promote rational use of medicine and excel in patient care servicesthrough establishment of therapeutic drugmonitoring unit, pharmacovigilance enter under PvPI and drug information centre

Suspected adverse drug reaction reporting form



SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by Healthcare Professionals

INDIAN PHARMACOPOEIA COMMISSION

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

FOR AMC/NCC USE ONLY

AMC Report No. :

Worldwide Unique No. :

A. PATIENT INFORMATION

1. Patient Initials ..... 2. Age at time of Event or Date of Birth _____ 3. M ☐ F ☐ Other ☐ 4. Weight_____Kgs

12. Relevant tests/ laboratory data with dates

B. SUSPECTED ADVERSE REACTION

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

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

7. Describe reaction or problem

13. Relevant medical/ medication history (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/renal dysfunction etc.)

14. Seriousness of the reaction (Yes ☐ No ☐)
☐ Death (dd/mm/yyyy) ☐ Congenital anomaly
☐ Life threatening ☐ Required intervention to Prevent permanent impairment/damage
☐ Hospitalization/Prolonged ☐ Other (specify)
☐ Disability

15. Outcomes
☐ Recovered ☐ Recovering ☐ Not recovered
☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S)

S.No	8. Name (Brand/Generic)	Manufacturer (if known)	Batch No. / Lot No.	Exp. Date (if known)	Dose used	Route used	Frequency (OD, BD etc.)	Therapy dates: Date started	Therapy dates: Date stopped	Indication
i										
ii										
iii										
iv										

S.No as per C	9. Action Taken: Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown	10. Reaction reappeared after reintroduction: Yes	No	Effect unknown	Dose (if reintroduced)
i										
ii										
iii										
iv										

11. Concomitant medical product including self medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

D. REPORTER DETAILS

16. Name and Professional Address: _____

Pin: _____ E-mail _____

Tel. No. (with STD code) _____

Occupation: _____ Signature: _____

17. Causality Assessment:

18. Date of this report (dd/mm/yyyy):

Additional Information:

Confidentiality: The patient's identity is held in strict confidence and protected to the fullest extent. Programme staff is not expected to and will not disclose the reporter's identity in response to a request from the public. **Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction.**

Assessment of pharmacovigilance

Standardised causality assessment

- WHO system
- French system

Data assessment in Pharmacovigilance

1. Individual case report assessment
2. Aggregated assessment and interpretation

- Signal detection
- Interactions and risk factors
- Serial (clinicopathological) study
- Frequency estimation

Data of a signal

- Qualitative (clinical)
- Quantitative (epidemiological)
- 'Experimental'
- Develops over time

The PRAC is responsible for assessing all aspects of **risk management** of human medicines, including.

the detection, assessment, minimisation and communication of the risk of adverse reactions, while taking the therapeutic effect of the medicine into account; design and evaluation of post-authorisation safety studies; pharmacovigilance audit.

The assessment tool is modular and classified to guide the selection of the most relevant indicators for the every unit of the health system. This supports the idea that pharmacovigilance should be developed only to meet a country's level of development and key priorities. The tool focuses on significant issues related to health systems that are recognized as the key factors in the overall capacity and sustainability of a medicine safety system.

Limitation

IPAT has the following limitations.

- The sensitivity and specificity of the indicators are not established.

- Non-medication-related patient safety indicators are not included.

About the IPAT Manual

The IPAT indicators are classified as follows.

A. Components—The components represent the elements of a functional pharmacovigilance system, including.

1. Policy, law, and regulation
2. Systems, structures, and stakeholder coordination
3. Signal generation and data management
4. Risk assessment and evaluation
5. Risk management and communication Indicators are numbered according to these components.

B. Core/Supplementary—Indicators are classified based on importance or how essentialthey are to a functional pharmacovigilance system. The most essential indicators are classified as Core, and others are classified as Supplementary.

C. Type of Indicator—Indicators are also classified based on the product or result they are measuring: structural, process, and outcome indicators.

- Structural: measures systems and physical infrastructures
- Process: measures how the pharmacovigilance system works
- Outcome: measures the final product of all the inputs into the pharmacovigilance activities

D. Data Collection Level—Indicators are classified according to the health system levelwherethey are relevant and could be collected.

- Ministry of Health (MoH) headquarters, which represents any data that can be collected at the national level, including the medicines regulatory authority. Also, depending on the indicator, data can be collected from the national pharmacovigilance center, pharmaceutical services, pharmaceutical companies, health professions university departments and associations.
- Public Health Program (PHP) represents specialized health programs such as the HIV/AIDS, tuberculosis (TB), malaria, vaccination, and maternal and child health programs.
- Health facilities (HFs) include primary, secondary, and tertiary or referral hospitals that providedirect services to patients. The point of data collection at the health facility may be the drug and therapeutics committee (DTC), pharmacovigilance unit, quality assurance

unit, patient safety or medication safety unit, infection control unit, and other similar units or departments of the clinic,health center, or hospital.

The indicator's data collection level classification can be used as a guide for determining which indicators are relevant to a particular unit of the health system. For example, the medicine regulatory authority will be interested in all indicators classified as MoH.

E. Recommended frequency of measurement—Indicators are classified according to the recommended frequency of data collection. For example, indicators related to policies and legislation are recommended to be collected every five years, allowing adequate time to review such documents and update them to current realities. Other indicators are recommended to be collected every year. Some of these indicators, particularly the structural ones, require subsequent monitoring that involves judgment of the current relevance of what is being measured.

Sampling and Data Collection

Identification of samples for administering the tool should take into consideration each country's realities. The regulatory authority should be assessed. All the public health programs and other stakeholders involved in pharmacovigilance at the national level will also need to be assessed. The data collection tool for public health programs is attached as annex 6. A single indicator relates to the universities or academic institutions and to the health professions council and associations. Depending on the number of academic institutions that offer training for health professionals, a representative number can be chosen. The same applies for the pharmaceutical companies and marketing authorization holders (MAHs) operating in the country. The data collection tool for national drug authority (NDA), pharmacovigilance center, and other nationallevel institutions is attached as annex 7. For the indicators addressing safe use of medicines at the health facilities, 10–15 health facilities may need to be sampled to obtain representative data. The health facilities should represent all levels of health care delivery. The data collection tool for the assessment of health facilities is attached in annex 8.

Conclusions from Assessment

Findings For a country to be regarded as having a minimally functional pharmacovigilance and medicine safety system, it must achieve all the core indicators. Subsequently, achievement of the supplementary indicators can indicate the sophistication of development of the country's medicine safety system.

Evaluation of the data

The evaluation of the available pharmacovigilance data consists of two parts. The BCPH evaluates the individual reports of adverse effects (spontaneous reports and SUSARs) but also evaluates the summary reports.

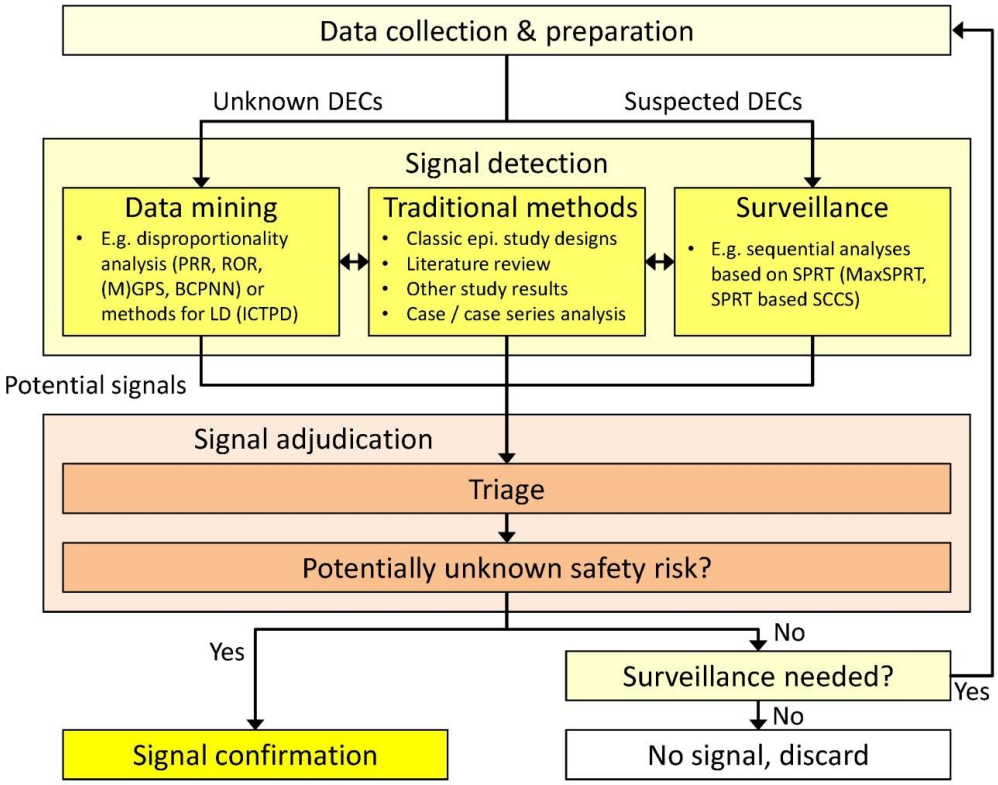
- periodic safety reports concerning a medicine;
- annual safety reports concerning a clinical trial (in case of medicines disposing already of amarketing authorisation);
- specific safety reports.

For these tasks, the BCPH is assisted by a team of internal and external experts. The individual reports are evaluated at regular intervals by a specific working group. The evaluation reports about periodic safety reports and the marketing authorisation renewal dossiers are submitted toa second specific working group. In case of medicines for which the responsibility for the evaluation is at national level, it is the Commission for Medicines for Human Use that gives the final advice about whether or not the measures suggested by the two working groups can be implemented. Based on the conclusions of these evaluations on national and European level, theBCPH takes the necessary measures.

One of the ways of collecting data for pharmacovigilance purposes is by providing a portal for drug users to provide information about their experiences with the drugs. This could be in the form of a special website that is easily accessible and easy to use. It may be difficult to convinceall drug users to log negative experiences of the drugs on the online portal, but the data collected from the few who do can be valuable.

Input from primary care physicians can also be used for pharmacovigilance purposes. When the doctors prescribe such medication, they usually have the responsibility of following up their patients to monitor their progress. If a side effect is noted and attributed to the drug in question, this can be brought to the attention of the party doing pharmacovigilance. For this to be effective, the primary care physicians will need to be sensitized on the need for this information, what to look out for and how to log the information.

Pharmacovigilance data can also be collected directly from patients who are receiving the drugs from hospital. This is particularly effective for IV medication, which needs to be provided withina hospital for safety purposes. An individual can then be delegated to collect data regarding theside effects that the patients have had as a result of using the drug.



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