WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 19, 1304-1315. Review Article ISSN 2277–7105

A COMPARATIVE STUDY OF REGULATORY ISSUES ON PHARMACOVIGILANCE IN US, EUROPE AND IN INDIA

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Article Received on
20 September 2023,

Revised on 10 Oct. 2023,
Accepted on 30 Oct. 2023

DOI: 10.20959/wjpr202319-30142

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ABSTRACT

The primary focus of the pharmacovigilance (PV) practice has been on the collection, assessment, and reporting of the adverse drug reactions to medicinal products. Globalization of the pharmaceutical industry has prompted efforts to toward harmonization of PV practices worldwide to enable improved knowledge of medicine's benefit-risk profile and risk communication. Even as PV has evolved over the past decade, there still exist few areas of discordance across global PV practices. This article compares the PV legislation in the United States, United Kingdom, Canada, and India with a view to understand areas of harmony in the current legislation across regions and further compare health authorities' requirements with recommendations made by international organizations. Identification of potential areas of disharmony would pave the way to design solutions and strategies toward creation of a comprehensive PV system, which can be easily implemented across the globe, thus promoting the safer use of medicines.

KEYWORDS: Adverse drug reaction, Drug safety, Harmonization, Pharmacovigilance.

1. INTRODUCTION[1-4]

Pharmacovigilance heavily focuses on adverse drug reactions, or ADRs, which are defined as any response to a drug which is noxious and unintended, including lack of efficacy. Information received from patients and healthcare providers via pharmacovigilance agreements (PVAs), as well as other sources such as the medical literature, plays a critical role in providing the data necessary for pharmacovigilance to take place. In fact, in order to market or to test a pharmaceutical product in most countries, adverse event data received by

the license holder (usually a pharmaceutical company) must be submitted to the local drug regulatory authority. Ultimately, pharmacovigilance is concerned with identifying the hazards associated with pharmaceutical products and with minimizing the risk of any harm that may come to patients. Companies must conduct a comprehensive drug safety and pharmacovigilance audit to assess their compliance with worldwide laws, regulations, and guidance Pharmacovigilance, often considered a key component in an effective drug regulation system, is a dynamic and constantly evolving scientific discipline. It is an umbrella term that describes the processes that are involved in evaluating and monitoring Adverse Drug Reactions (ADR's). The World Health Organization (WHO) defines Pharmacovigilance as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems. In India, all social insurance experts including specialists, medical caretakers, and drug specialists can report an ADR by filling an ADR type of the Central Drugs Standard Control Organization. The dynamic interest of social insurance experts in the pharmacovigilance program can enhance the ADR revealing. In India, National Pharmacovigilance Centre (NPC) has been formed which is an active participant in the on-going activities of UMC and in the past years, the PV programme has gained momentum such that the reporting rates from India have increased from 5% to 20%.

Main areas of Pharmacovigilance

Pharmacovigilance is a huge and encompassing discipline, but we can broadly divide pharmacovigilance into four main sub-specialisms.

Operations

This sector is where many life science professionals interested in drug safety jobs will begin their career. Typical jobs within drug safety operations include case processor, drug safety officer/associate and drug safety manager, and of course team lead and directorships. These professionals will collect and record information during preclinical development and clinical trials, in addition to gathering real world evidence (RWE) of adverse events reported by doctors and patients post-market. Operations are also usually responsible for creating standard operating procedures (SOPs), individual case study reports, literature screening and regulatory expedited reporting.

Surveillance

Professionals who focus more within surveillance tend to look towards risk management and signal detection jobs. This also involves performing analysis of the data collated by the wider division. Professionals in this area can hold an array of titles, the most common of which are pharmacovigilance scientist and drug safety physician, but like in all teams, there are many degrees of seniority and remit available. These professionals perform analysis on the drug safety information gathered by the wider department and assist with the creation and review of aggregate reports. They also create development safety update reports (DSURs) for drugs in clinical research, and periodic benefit risk evaluation reports (PBRER) for post-market drugs. These reports ultimately help the team to draw conclusions around the safety and efficacy of a drug or candidate molecule.

Systems

This division is concerned with the building and ongoing development of a fully robust and innovative system, charged with the responsibility for housing and allowing access (in various forms) to vast quantities of safety data. This safety data is usually collated by those working in operationally focused roles, but is accessed by all. The systems division constantly has to improve, and stay in line with, changing regulations and requirements for the business/ health authorities, making this a very challenging and vital aspect of drug safety.

Qualified Person for Pharmacovigilance (QPPV)

QPPVs jobs are mainly concerned with marketed drugs and those about to be authorised, but as QPPVs are considered by many to be subject matter experts, their expertise is utilised across the discipline and wider business. These senior pharmacovigilance roles will only be held by very experienced professionals and their focus is to understand, plan for and advise upon the regulations and requirements that companies must adhere to across the EU. This is a highly strategic appointment and one of great importance. Fortunately for drug safety professionals, there are several pharmacovigilance jobs available to them due to the different types of companies within life sciences, including global pharmas, small pharmas, generics companies, drug safety consultancies and health authorities. Each offers slightly different opportunities but in every case, there is plenty of scope for professionals to progress their pharmacovigilance career.

Importance of Pharmacovigilance

Patient safety and continuous vigilance

Power and authority

Adverse event reporting

Individual Case Safety Report (ICSR)

USFDA

This document provides guidance to industry on good pharmacovigilance practices and pharmacoepidemiologic assessment of observational data regarding drugs, including biological drug products (excluding blood and blood components) and also the following.

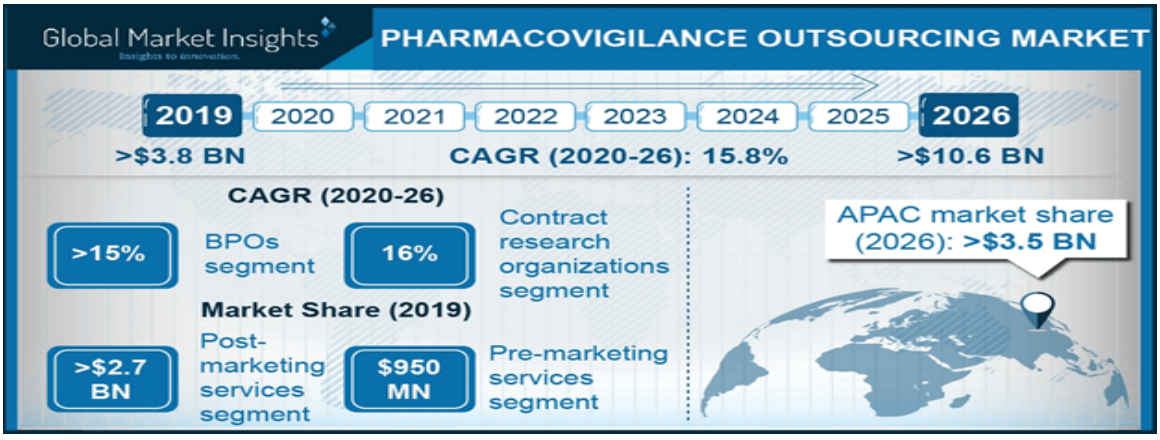
- ✓ Safety signal identification,
- ✓ Pharmacoepidemiologic assessment and safety signal interpretation, and
- ✓ Pharmacovigilance plan development.

EMA

Good pharmacovigilance practices (GVP) for the European Union A set of guidelines for the conduct of pharmacovigilance in the EU, drawn up based on Article 108a of Directive 2001/83/EC, by the European Medicines Agency in cooperation with competent authorities in Member States and interested parties, and applying to marketing authorisation holders in the EU, the Agency and competent authorities in Member States.

INDIA

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 2010.11.



2. METHODOLOGY[5-13]

Pharmacovigilance Programme of India (PvPI)

The Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services under the aegis of Ministry of Health & Family Welfare, Government of India in association with Indian Pharmacopeia commission, Ghaziabad is initiating a nation-wide Pharmacovigilance Programme for protecting the health of the patients by promising drug safety. The Programme shall be coordinated by the Indian Pharmacopeia commission, Ghaziabad as a National Coordinating Centre (NCC). The center will operate under the supervision of a Steering Committee. 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 safe-guarding Public Health. In the year 2010, 22 ADR monitoring centres including AIIMS, New Delhi was set up under this Programme. To safeguard implementation of this programme in a more effective way, the National Coordination Centre was shifted from the All India Institute of Medical Sciences (AIIMS), New Delhi to the Indian Pharmacopoeia Commission, Ghaziabad, Uttar Pradesh on 15th April 2011.23.

Mission: Safeguard the health of the Indian population by ensuring that the benefits of use of medicine outweigh the risks associated with its use.

Vision: To improve patient safety and welfare in Indian population by monitoring the drug safety and thereby reducing the risk associated with use of medicines.

OBJECTIVES

- To create a nation-wide system for patient safety reporting.
- To identify and analyze the new signal (ADR) from the reported cases.
- To analyses the benefit - risk ratio of marketed medications.
- To generate the 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 minimize the risk
- To emerge as a national center of excellence for pharmacovigilance activities.
- To collaborate with other national centers for the exchange of information and data management.

• To provide training and consultancy support to other national pharmacovigilance centers located across globe.

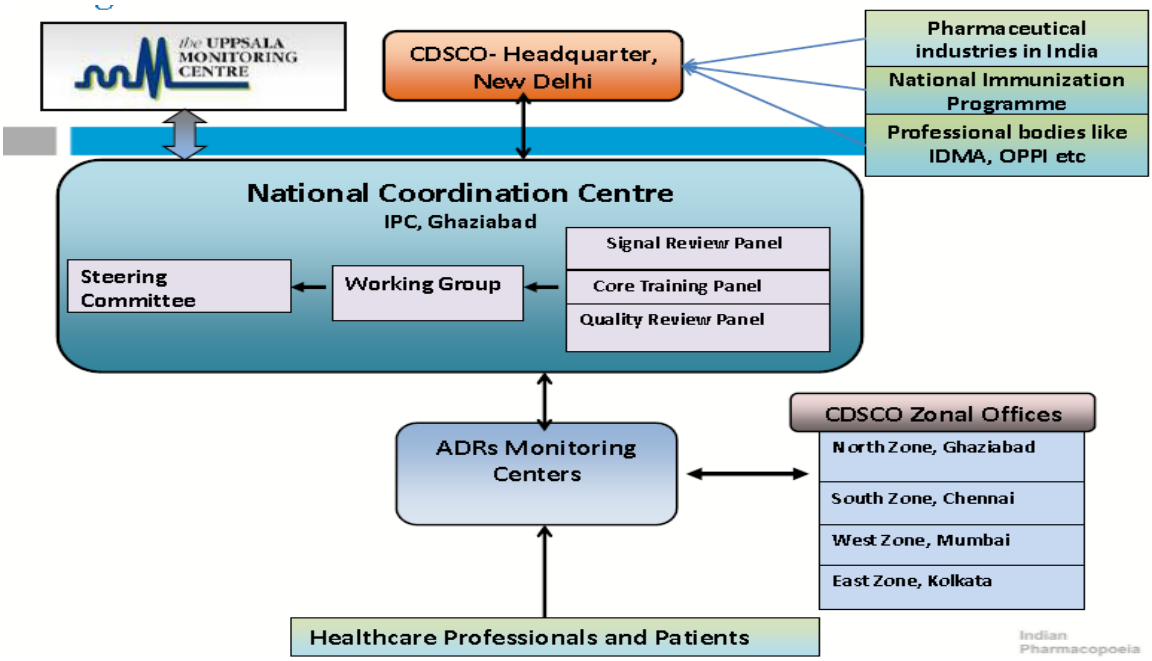


Fig-1: Pharmacovigilance Programme of India (PvPI).

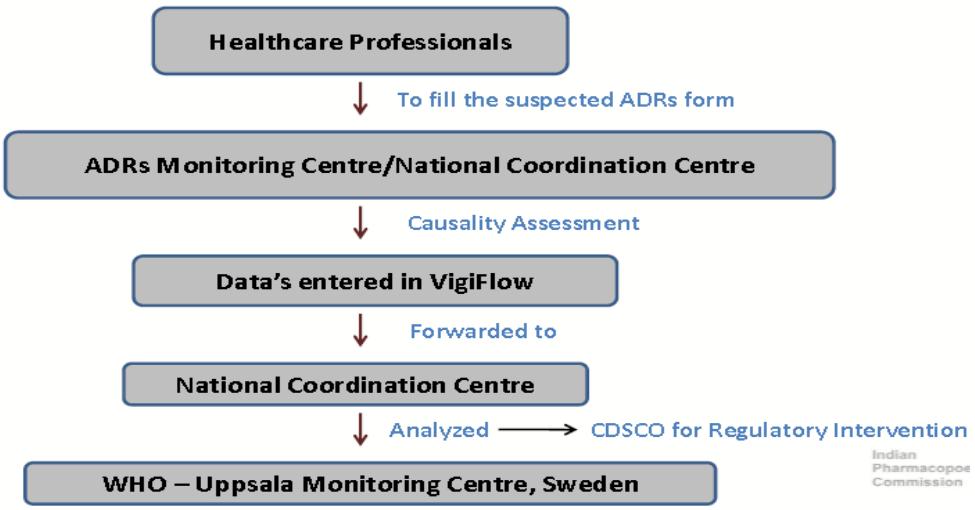


Fig-2: Collection, analysis and evaluation of ADRs.

Pharmacovigilance Programme of US (USFDA)

A key component of the FDA mission is to protect the public health by assuring the safety of human drug products. Supporting this objective, FDA is also responsible for advancing public health by facilitating the scientific innovations that can help make medicines safer while assuring that the public receives clear, accurate, science-based drug safety messages.

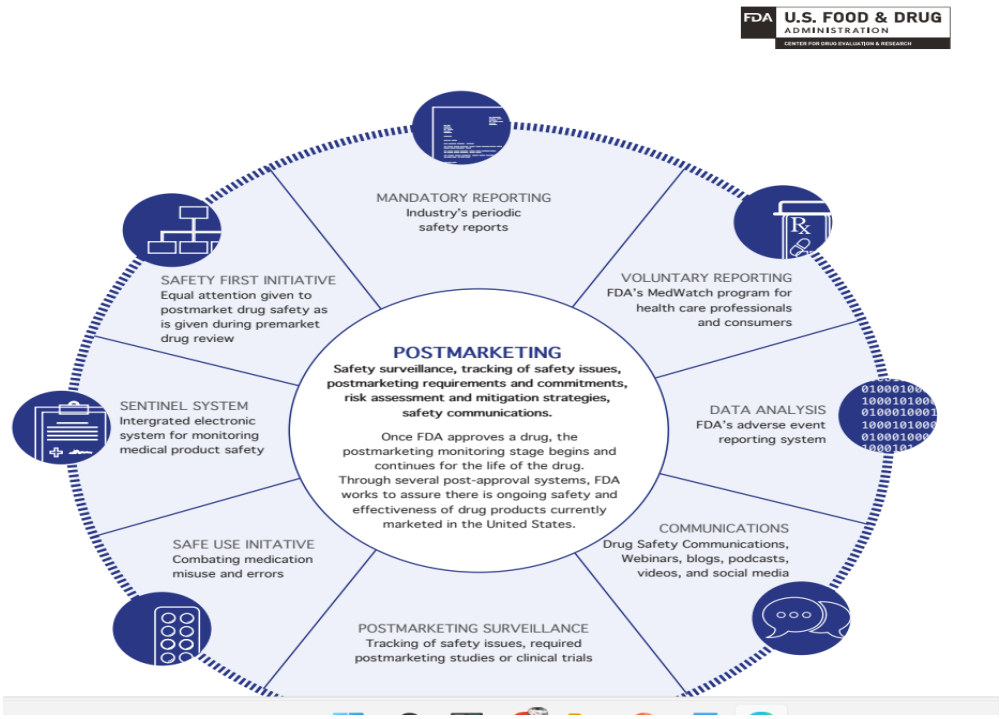
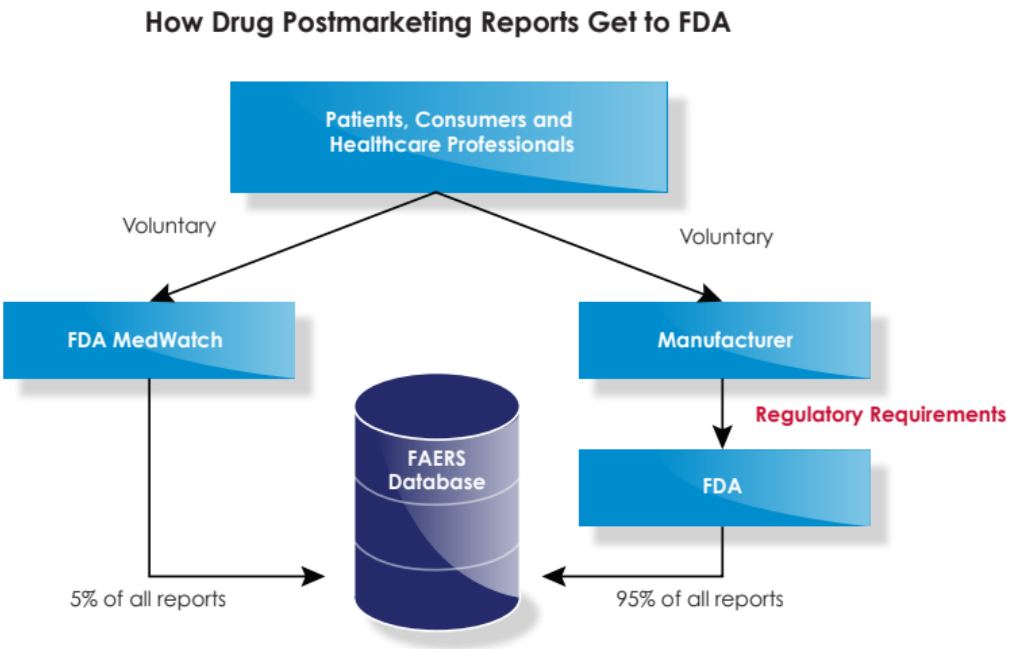


Fig 3: Pharmacovigilance Programme of US (USFDA).



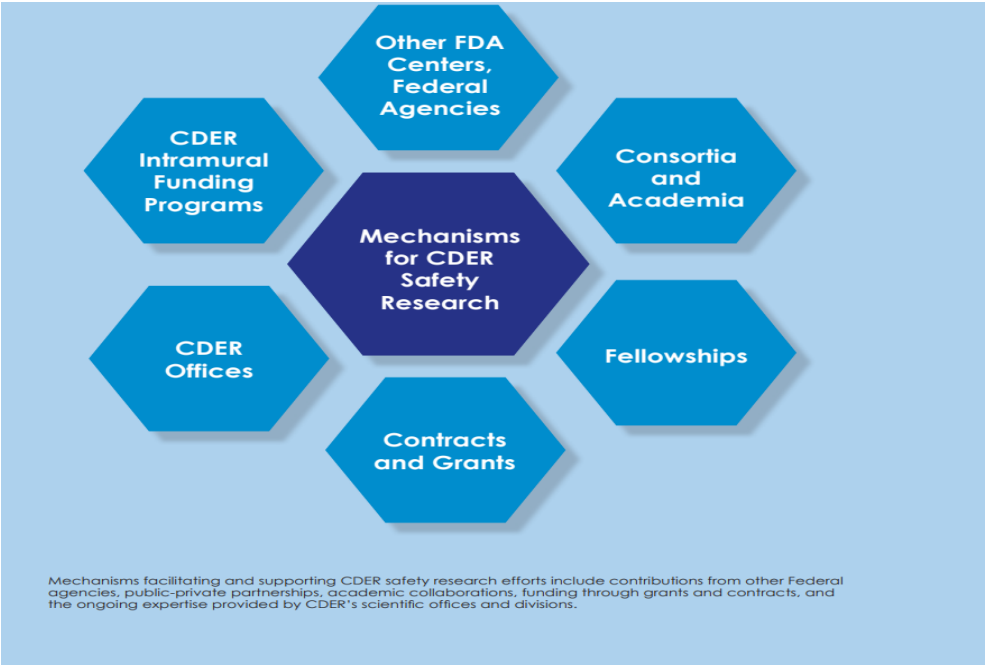


Fig-4: MedWatch is FDA's system for the reporting and collection of clinically important safety information about marketed human medical products.

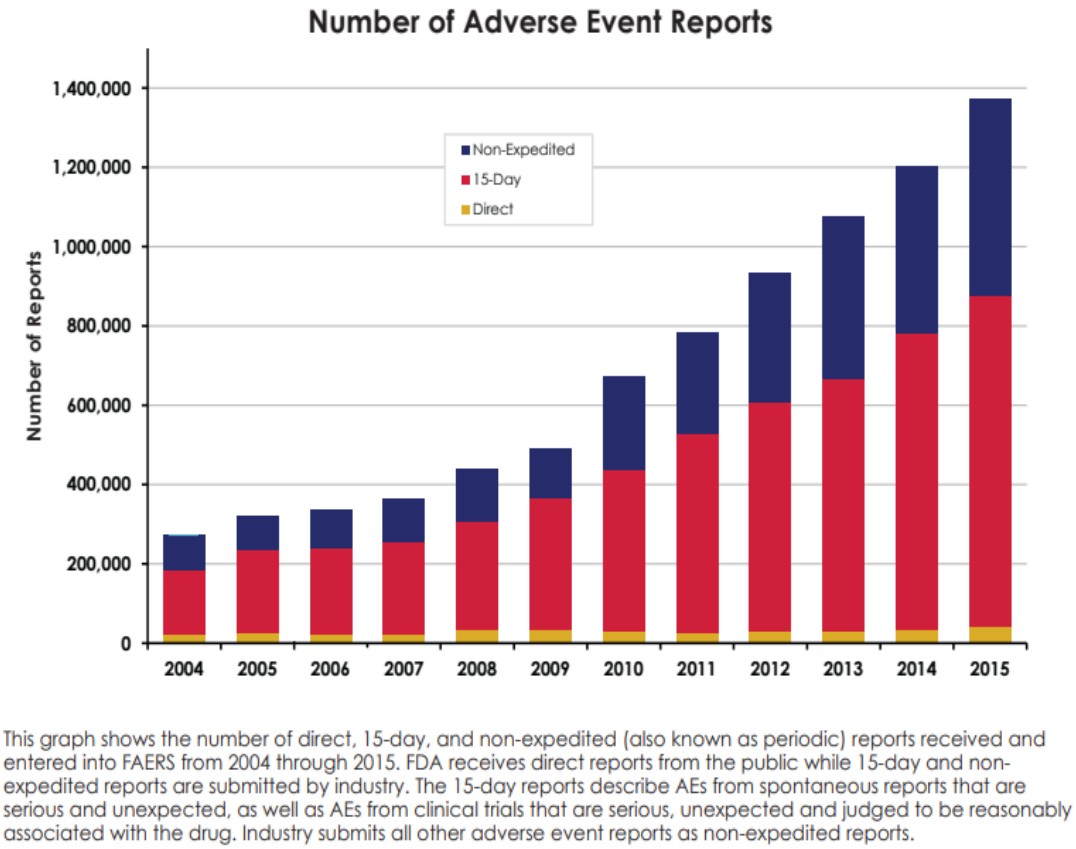


Fig 5: Number of Adverse Event Reports.

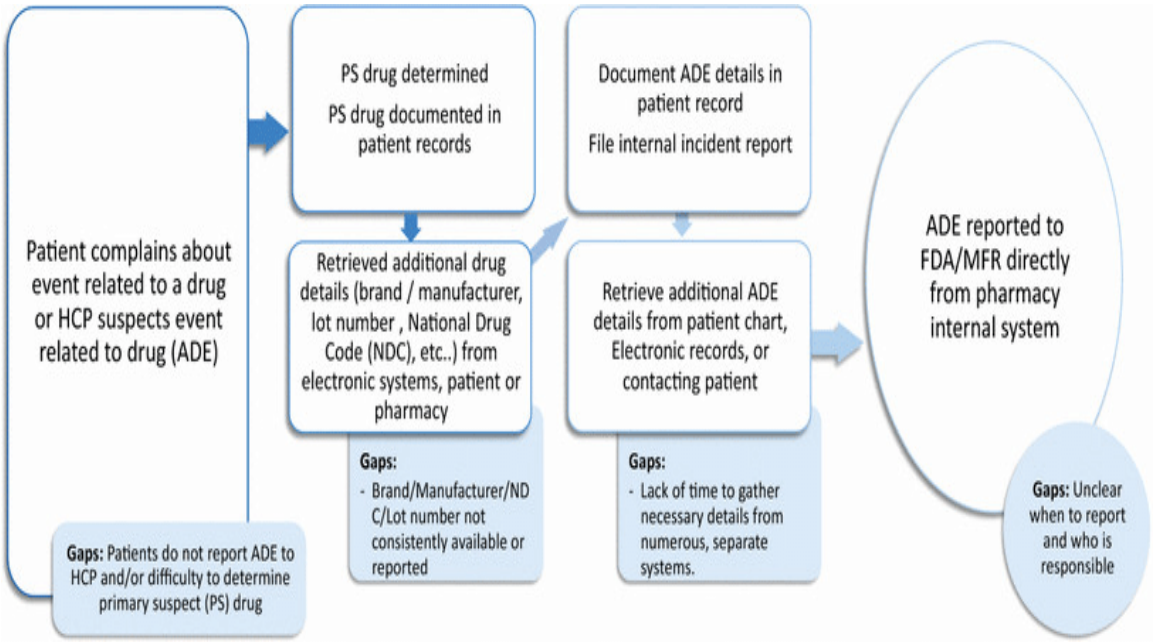


Fig 6: ADR reporting USFDA.

3. EMA PHARMACOVIGILANCE SYSTEM

In accordance with the provisions of European Union (EU) legislation relating to medicinal products, the EMA is the EU body responsible for coordinating the existing scientific resources put at its disposal by Member States for the evaluation, supervision and pharmacovigilance of medicinal products.76

The EMA is responsible, in particular, for.

• providing independent, science-based recommendations on the quality, safety and efficacy of medicines, and on more general issues relevant to the promotion and protection of public health that involve medicines;

• implementing measures for continuously supervising the quality, safety and efficacy of authorised medicines to ensure that their benefits outweigh their risks;

• publishing impartial and comprehensible information about medicines and their use;

• developing best practice for medicines evaluation and supervision in Europe, and contributing alongside the Member States and the European Commission to the harmonisation of regulatory standards at the international level.

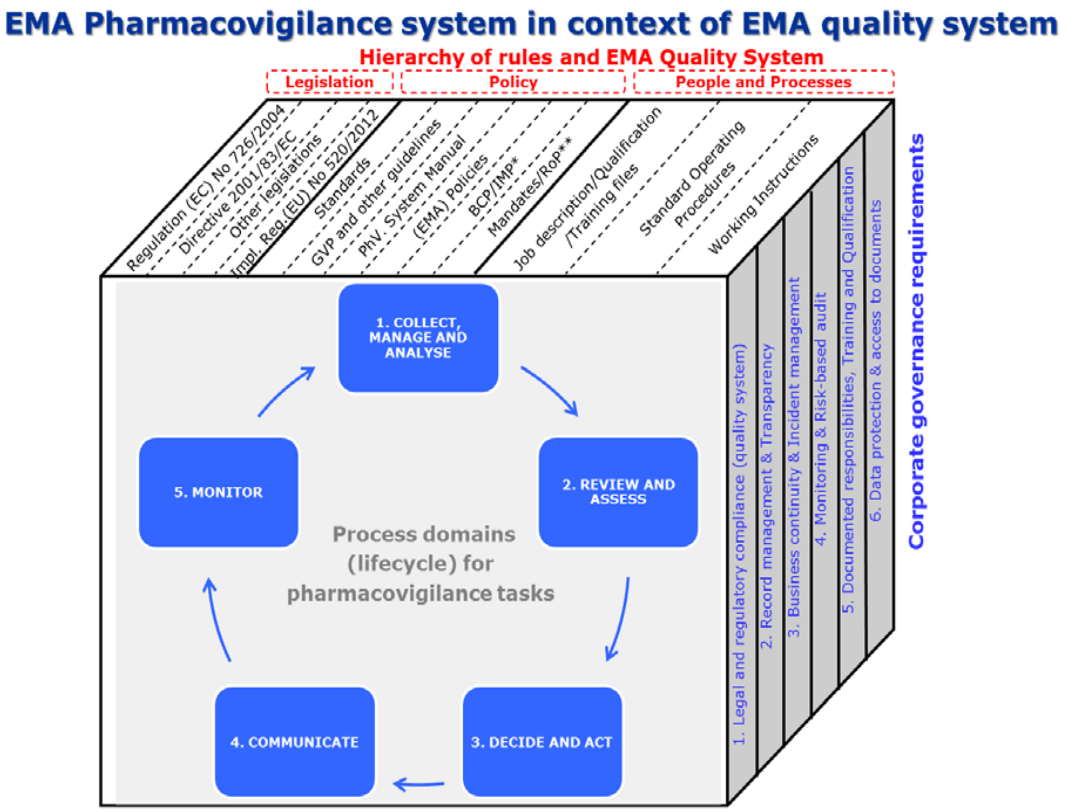


Fig 7: The EMA pharmacovigilance system in the context of the EMA quality system.

4. CONCLUSION

Drug toxicity is a relatively common phenomenon—despite a stringent drug safety and clinical trials process, several drugs have been removed from the market being approved by National Drug Regulatory Authorities, including US' FDA, UK's MHRA, and Europe's EMEA [refer to annex of drug withdrawals]. In addition to the removal of potentially toxic drugs from the market, one out of every five drugs are required to add additional warnings related to side effects, contraindications, etc. Globally, only about 500,000 to 700,000 adverse event occurrences are captured each year—however, low to middle income countries, which represent more than two thirds of the world's population account for a tiny fraction of all the ADR data.

National Program of Pharmacovigilance was launched in 2005, and was renamed as the Pharmacovigilance Program of India (PvPI) in 2010. In consideration of having a robust pharmacovigilance system in India, steps were taken.

The program is striving hard to build trust between the physician and the patient, thereby increasing patient safety and the confidence of people in the country's health system, in addition to the detection of substandard medicines and prescribing, dispensing and

administration errors. The IPC-PvPI has now become a WHO Collaborating Centre for Pharmacovigilance in Public Health Programmes and Regulatory Services. The below areas should develop in their aspects for better pharmacovigilance program in India.

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