



REVIEW ARTICLE

Global Pharmacovigilance, challenges, and future considerations: West globe and East globe

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ARTICLE INFO ABSTRACT



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Introduction: Pharmacovigilance (PV) plays a consequential role in the drug regulatory system and is a constantly evolving multifaceted field. In the process of carrying out its effective management, the PV system does undergo a lot of challenges on a global pitch. PV system is well developed in the western globe (United States, United Kingdom, Germany) while the east globe (e.g.: India) is still in the evolving stage.

Methods: Major discrepancies include different regulatory authorities for each nation with different forms for ADR reporting and also different timelines.

Results: To mention a few; there is a regulatory gap because of the continuously evolving regulations and business processes, it is difficult to comply with the diverse regulations effectively; gross underreporting in the east as compared to the west; increased concern about the safety and potential toxicity of traditional Chinese herbs in the east; self-medication; linguistic barrier, etc. Steps like harmonization of regulation by drafting guidelines that are uniform globally; leveraging digital technologies to optimize ADR reporting; meticulous and timely reporting; inclusion of PV in the curriculum etc. can be employed.

Conclusions: While PV has witnessed substantial development over the years, areas of discrepancies need to be identified to build a seamless PV system. Need for an effective revolutionary roadmap to tackle all the hindrances to fortify its harmonious functioning.

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Introduction

Pharmacovigilance (PV) plays a consequential role in the drug regulatory system and is a constantly evolving multifaceted field. The World Health Organisation (WHO) defines PV as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems." It helps in identifying adverse drug reactions (ADR) thus improving patient care and safety and also encouraging safe, rational, and effective use of medicines from both

therapeutic and economic frames of reference (Fernandes *et al.*, 2018).

There are mainly 4 cornerstones involved in the PV system which have been proved effective in safeguarding public health. They are

- Collection of ADR through various sources
- Analysis and understanding of the data and information
- Communication with all stakeholders
- Regulatory action for public health protection.



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In the process of carrying out the effective management of these cornerstones, the PV system does undergo a lot of challenges on a global pitch.

PV in the West globe

PV in the western globe particularly United States(US) and Europe which are the first and second-largest pharmaceutical markets in the world respectively are well developed because of their well-established regulatory bodies which have laid out clear PV functioning and

reporting requirements. On the other hand, in the east globe particularly Asia which is the third-largest pharmaceutical market in the world (Japan, China, India) national regulators, as well as their respective regulations, are still evolving (Biswas P, 2013).

The major differences between PV regulations in the West and East globe are given below in Table 1 (Jose et al., 2019; Hans and Gupta, 2018; Hori et al., 2011).

Table 1: Comparison of PV Systems

Sr. No.		Unites States	Europe	Japan	China	India
1	Regulatory authority	FDA	EMA	PMDA and MHLW	CNDA and MOH	CDSCO
2	PV authority	CDER/CBER	EVDAS	PMDA	CNDA	NCC-IPC (PvPI)
3	Guidelines followed	GVP and Pharmacoepidemiologic assessment	GVP	ICH-E2A	ICH-2EA	Schedule Y
4	Online ADR reporting software	MedWatch	Eudravigilance	PMDA database	Chinese ADR database	Vigiflow
5	PV database	FAERS Sentinel system	EVDAS, EVWEB	JADER database	CADRMS	Vigibase
6	ADR form types	3 forms: a)3500 b)3500A c)3500B	Yellow card ADR form	Online spontaneous reporting system	Online spontaneous reporting system	2 forms: a)HCP b)Consumer
7	PSUR timeline	15-day alert reports, quarterly for the first 3 years and annually thereafter	First two years- every 6 months, once a year for two consecutive years once in 3 years thereafter	Every 6 months for the first 2 years and annually later	Annually for the first 5 years then every 5 years	First 2 years –every 6 months once a year for 2 consecutive years and thereafter annually

FDA-Food and Drug Administration, EMA-European Medicines Agency, PMDA-Pharmaceuticals and Medical Devices Agency, MHLW-Ministry of Health, Labour and Welfare, CNDA-China Nation Drug Administration, MOH-Ministry of Health, CDSCO-Central Drugs Standard Control Organization, CBER-Center for Biologics Evaluation and Research, CDER-Center for Drug Evaluation and Research, EVDAS-European Commission, Eudravigilance Data Analysis System, GVP-Good Pharmacovigilance Practices, FAERS- FDA Adverse Event Reporting System, ICH- International Council for Harmonization, PSUR- Periodic Safety Update Report, JADER-Japanese Adverse Drug Event Report, CADRMS- Chinese Adverse Drug Reaction Monitoring System, NCC-IPC- National Coordination Centre-Indian Pharmacopoeia Commission]

The Challenges

Table 2: Challenges in PV systems in West and East Globe

West Globe	East Globe
Regulatory gap because of the continuously evolving regulations and business processes, it is difficult to comply with the diverse regulations effectively	Gross underreporting due to lack of awareness among HCP and consumers, excess workload lack of medical expertise, lack of motivation, and the wide time interval

(Beninger P, 2018).

Encouraging collaboration of PV centers with public health authorities to ensure ADR reporting is done at the right time and does not hinder access to essential medicines. (Dal Pan *et al.*, 2014).

System integration by maintaining high levels of data quality and privacy (Dal Pan *et al.*, 2014).

Lack of resources (people, time, money) in comparison with the growing proportion of available data.

Self-medication: In the current era of the internet where everything is available on the internet, over-the-counter drug consumption has increased significantly creating a new challenge for PV (Fernandes *et al.*, 2018).

Social media: Difficult to interpret layperson terminologies i.e. inability to identify the patient reporter which raises ethical concerns and regulatory issues (Sloane *et al.*, 2015).

between timelines and laws (Mittal *et al.*, 2016).

In fixed drug combinations, it is difficult to establish a temporal relationship between the drug and ADR (Kalaiselvan *et al.*, 2018).

Self-medication (Fernandes *et al.*, 2018).

Careful monitoring of generic drugs and biosimilars- Need of guidelines (Kalaiselvan *et al.*, 2018).

Fear- As India is a growing hub for clinical trials, an increase in them has led to an increase in ADR but these go under-reported to the concerned authority in the fear of legal actions (Fernandes *et al.*, 2018).

Lack of government funds to run the program efficiently (Biswas P, 2013).

Traditional and herbal Chinese medicines have always been an important part of healthcare and there has been increased concern about their safety and potential toxicity (Zhang *et al.*, 2014).

Collaboration with the IT sector.

Orthodox attitude to new drug research (Mittal *et al.*, 2016).

Linguistic barrier-challenge at different stages of PV in terms of global exchange of information (Zhao *et al.*, 2018).

Discussion

Comparing the specific components of the PV system namely PV regulation, regulatory authority, and processes across the west and east globe (US, UK, India, China, Japan) shows many areas of dissonance. Major discrepancies include different regulatory authorities for each agency with different forms for AR reporting and also different timelines. Being the largest pharmaceutical market, there is disharmony in many areas which need to be assessed and worked upon to bring a robust and compendious PV system ensuring international harmonization. The deficiencies that our study identified confront low- and middle-income countries which are less of a constraint in developed countries. A strong PV system is a crucial part of the overall medicines regulatory system which indicates the rigor and competence of the regulatory bodies in fulfilling their responsibilities for oversight of producers and markets (Hans and Gupta, 2018). Understanding what is a safety concern versus a crisis and what is required for reporting safety information between industry and regulators would help in minimizing miscommunications and help in maintaining greater worldwide drug safety and utilization. The WHO, The ICH of Technical Requirements for Registration of Pharmaceuticals for Human Use, and the CIOMS and their efforts toward harmonization of pharmaceutical regulation specific to PV and towards safer medicines are of great

importance. They have made great strides toward coalescing PV practices globally but a level of complete harmonization of the adverse event reporting systems and risk management strategies does not yet exist (Andrews *et al.*, 2006).

Future considerations

While PV has witnessed substantial development over the years, areas of discrepancies need to be identified to build a seamless PV system with sustained efforts. This is a collaborative venture which requires the teamwork of HCP, patients, and stakeholders to build an efficient and stringent PV setup.

The following considerations can be employed going forward-

- Harmonization of PV legislation-Drafting of guidelines for ADR reporting which are uniform globally.
- Adopting 'Generic ADR form' worldwide mandatorily for reporting of any/all ADRs (Singh *et al.*, 2012).
- Shifting from Big data to Smart data- This will strengthen PV network and improve operating PV capabilities and collaborative working in terms of coordination, communication, evaluation, and assessment of ADR reporting, signal management, and quality assurance

management thus causing standardization of PV processes (Dal Pan *et al.*, 2014).

- Volume to Value-Leveraging digital technologies like machine learning, natural language processing (NLP), robotic process automation, application programming interface (API) to optimize reporting of adverse events.
- Expand the involvement of regulators and manufacturers with professional and academic institutions, patient-based organizations, financial institutions, and IT sectors.
- Building up of the foundation with EU2P model (European training program in pharmacovigilance and pharmacoepidemiology) which will help stakeholders in collaborating with academic institutions thus helping present PV professionals and new ones expand their skills. Introducing such programs in other regions/countries will help broaden the horizon of existing PV (Fernandes *et al.*, 2018).
- Mandatory inclusion of PV course in the undergraduate curriculum.
- Training of the health personnel.
- Increase the number of ADR monitoring centers (AMC) where reporting centers are not available (Fernandes *et al.*, 2018).

Conclusions

PV is the most proficient tool to safeguard public health. By combined efforts and a streamlined approach, and effective revolutionary roadmap can be crafted to tackle all the hindrances to fortify its harmonious functioning. As Wallace and Evans have rightly said 'PV should operate in a culture of scientific development. This requires the right balance of inputs from various disciplines, a stronger academic base, and greater availability of basic training and resource which is dedicated to scientific strategy.

Conflict of Interest

No conflict of interest

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