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Regulatory Harmonization in Indian Pharmacovigilance: Convergence with Global Standards and Unique National Adaptations

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Abstract
Over the past ten years, India's pharmacovigilance (PV) environment has rapidly changed due to the country's requirement to fulfil international regulatory standards as a top pharmaceutical producer and to guarantee drug safety for its diverse population. India's changing PV regulatory framework has been influenced by the incorporation of international standards, including those from the European Medicines Agency (EMA), the World Health Organisation Programme for International Drug Monitoring (WHO-PIDM), the Council for International Organisations of Medical Sciences (CIOMS), and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Large-scale public health initiatives, patient populations with a variety of cultural backgrounds, and the existence of ancient medical systems like Ayurveda, Siddha, and Unani are just a few of the distinctive national adaptations that India has made in response to local healthcare circumstances.
The convergence of India's PV rules with international norms is examined in this review, which also identifies characteristics specific to India's regulatory framework. It examines significant accomplishments, details operational and structural changes, assesses enduring difficulties, and highlights prospects for further harmonisation in the future. The study emphasises that although India has made significant strides in implementing risk management, digital reporting, and international alignment, issues with underreporting, industry capacity fluctuation, insufficient active surveillance, and the requirement for legislative reforms still exist. Overall, the path towards harmonisation has improved India's standing internationally in the drug-safety ecosystem; but full global equivalency would require continued investment, digital growth, and regulatory modernisation.

Keywords: Regulatory Convergence, Harmonization, Pharmacovigilance, PvPI, ICH, WHO, Drug safety

1. Introduction
The increasing internationalisation of pharmaceutical research, development, and marketing has made drug safety regulation a complex, international endeavour. Since medications are sold internationally and clinical trials are carried out in multiple regulatory countries, harmonised pharmacovigilance (PV) systems are obviously required. Harmonisation promotes innovation and regulatory efficacy while safeguarding patient safety by guaranteeing that safety data are generated, evaluated, and distributed uniformly. As one of the world's biggest producers of medicines, a significant exporter of generic drugs, and a fast-expanding market for innovative therapies, India has emerged as a key hub in the global safety ecosystem. In addition

to being a strategic necessity, the nation's efforts to align its PV practices with international standards are a public health priority. (1)

India's PV regulation regime has changed especially quickly in the last ten years. Due to inadequate regulatory frameworks and limited healthcare professional awareness, spontaneous adverse drug reaction (ADR) reporting was previously distributed and underutilised in India. Due to these problems, India found it challenging to fully participate in international clinical research, international drug supply networks, and domestic patient safety procedures. Recognising these limitations, the Indian government launched the Pharmacovigilance Programme of India (PvPI) in 2010 as a long-term national initiative to improve safety monitoring, strengthen regulatory coordination, and build institutional capacity. PvPI created a large network of ADR Monitoring Centres (AMCs), standardised reporting processes, integrated digital technologies like the Vigiflow database, and set guidelines to guarantee adherence to the World Health Organization's (WHO) Programme for International Drug Monitoring. (1)

The country's regulatory transformation is increasingly mirroring the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) frameworks, particularly the E2 series of guidelines that govern clinical safety reporting, signal management, and risk assessment. Global regulatory paradigms that have been embraced in nations like the United States, Japan, Australia, and the European Union (EU) are reflected in India's implementation of Schedule Y changes, Good Pharmacovigilance Practices (GVP), and risk management regulations. When taken as a whole, these modifications strengthen India's reputation as a globally recognised regulatory agency capable of offering robust oversight throughout the whole pharmaceutical life cycle, from preapproval development to post-marketing surveillance. (1,2)

Because of India's own legal and ethical frameworks, including compensation processes for accidents related to clinical trials, PV standards must take into account both domestic regulatory limits and cultural expectations. The impacts of regulatory harmonisation are extensive. For the pharmaceutical industry, it promotes innovation, expedites global product development, and removes duplication in compliance processes. Harmonisation increases the international recognition of Indian clinical trial results and boosts India's competitiveness in regulated countries like Europe and North America. By giving regulators access to worldwide evidence, improving signal detection efficiency, and promoting risk communication, harmonisation speeds up decision-making. It lowers unfavourable outcomes, promotes an environment of transparency and attentiveness for patients and healthcare facilities, and aids in the early detection of safety signs. (2,3)

2. Historical Evolution of Indian Pharmacovigilance

Pharmacovigilance in India has gradually evolved from dispersed safety monitoring procedures to a centralised, structured system that complies with international regulatory requirements. Each stage of the evolution of contemporary pharmacovigilance governance was marked by particular institutional changes, legislative initiatives, and capacity-building initiatives. India launched its initial attempts to formalise drug safety surveillance in the 1980s, when spontaneous adverse drug reaction (ADR) reporting was erratic and primarily depended on the voluntary efforts of individual clinicians. There are limited legal restrictions and no centralised infrastructure for post-marketing surveillance (PMS). The Drugs Controller General of India (DCGI) released preliminary recommendations urging pharmaceutical companies to submit ADR data. However, implementation remained inconsistent because of a lack of laws and low knowledge among healthcare personnel. (3)

An important turning point occurred in 1997 when India joined the Uppsala Monitoring Centre (UMC)-run WHO Programme for International Drug Monitoring. India was admitted into a global network of drug safety surveillance through this integration, which gave it access to international ADR databases, reporting systems, and capacity-building facilities. Despite these developments, the low national reporting rate emphasises the need for a unified, government-led PV system. (3)

2.1 National PV Programme Establishment (2004-2010)

The Ministry of Health and Family Welfare launched the National Pharmacovigilance Programme (NPP) in 2004 with the goal of establishing a functional ADR monitoring network across major healthcare facilities. The program aimed to create zonal centres responsible for collecting, assessing, and forwarding ADR reports to the UMC. It was funded by the World Bank under the National Rural Health Mission. NPP improved national cooperation and created early ADR reporting experience, but a number of limitations persisted. Standard operating procedures varied amongst institutions, the reporting culture remained insufficient, and many centres lacked qualified personnel. The need for a more dependable and sustainable PV system became more apparent. (4)

2.2 Phase of PvPI (2014–2020)

The establishment of the Pharmacovigilance Programme of India (PvPI) under the Indian Pharmacopoeia Commission (IPC) in July 2010 marked a major turning point in India's PV history. PvPI developed a comprehensive and systematic approach to ADR monitoring that included a number of crucial elements: (4)

- Standardisation of reporting formats that adhere to WHO guidelines; establishment of ADR Monitoring Centres (AMCs) at hospitals and medical institutions to enable organised data collection.
- Digital reporting technologies such as VigiFlow make it simple to submit individual case safety reports (ICSRs) to the global WHO database (VigiBase).
- Capacity-building initiatives, such as training courses for doctors, nurses, and chemists.
- The establishment of specialised PV facilities, such as those focused on medical equipment, biologics, and vaccine surveillance. (4)

In the 2010s, India focused on formalising PV inside its regulatory framework. Among the significant developments were:

- Modifications to Schedule Y (clinical trial regulations) to tighten safety reporting.
- The installation of pharmacovigilance systems that marketing authorisation holders (MAHs) are required to utilise.
- The release of Good Pharmacovigilance Practices (GVP) recommendations in compliance with ICH and European Medicines Agency (EMA) recommendations.
- Using Periodic Safety Update Reports (PSURs) and signal management protocols in compliance with international guidelines.
- PvPI reporting has been extended to include medical devices, herbal products, and vaccines in response of the growing complexity of therapeutic categories. (5)

2.3 Digital and Regulatory Strengthening (2020–Present)

In recent years, the adoption of technology-driven and patient-focused PV advancements has accelerated:

- The ADR reporting mobile app, which enables individuals and practitioners to directly submit reports, was released.
- The introduction of e-reporting gateways for pharmaceutical companies.

- More thorough safety monitoring in public health initiatives is made possible by integration with national programs like Ayushman Bharat.
- A greater focus on risk management techniques (RMPs), post-authorization safety studies (PASS), and benefit-risk communication.

By emphasising the importance of real-time safety monitoring, especially for vaccinations, the COVID-19 pandemic spurred improvements in active surveillance and rapid signal evaluation systems. (5)

3. Global Regulatory Frameworks Relevant to India

India's pharmacovigilance environment has been greatly impacted by international regulatory frameworks that set standards for medication safety monitoring, reporting, and risk management. By adopting and altering a number of international principles, India, a major participant in the global pharmaceutical market and a member of numerous international regulatory bodies, has enhanced its Pharmacovigilance Programme of India (PvPI). In addition to guiding national policy, these global frameworks ensure data quality, interoperability, and harmonisation with international drug safety systems. (6)

3.1 World Health Organization-Uppsala Monitoring Centre (WHO-UMC)

The foundation of international pharmacovigilance cooperation is the WHO Programme for International Drug Monitoring (PIDM), which is handled by the Uppsala Monitoring Centre (UMC). After joining the PIDM in 1997, India fully integrated PvPI into its operational architecture. PvPI is used to create the VigiBase and VigiFlow platforms, which are utilised globally for ICSR processing; the WHO-UMC standards for ADR Monitoring provide basic standards for signal recognition, causality evaluation, and spontaneous reporting. The WHO's Good Pharmacovigilance Practices (WHO GVP) are followed in the development of India's standard operating procedures. WHO-ATC/DDD and MedDRA nomenclature enable India to use internationally known ADR categorisation systems. By ensuring that Indian safety statistics are globally comparable, these WHO guidelines promote worldwide sharing and signal detection. (7)

3.2 Collaboration of India with ICH

An important step towards bringing national PV regulations into compliance with international norms has been India's cooperation with ICH. Since becoming an official member of the ICH, India has progressively complied with significant criteria, particularly those found in the ICH E2 series. Combining Indian PV with ICH Guidelines:

- ICH E2A (Clinical Safety Data Management): It sets rules for promptly reporting serious and unexpected adverse medication events. (8)
- ICH E2B (Electronic Transmission of ICSRs): India adopted ICH E2B (Electronic Transmission of ICSRs) (R3) standards for systematic and uniform electronic reporting. (11)
- ICH E2C(R2) (Periodic Benefit-Risk Evaluation Report): ICH E2C(R2) (Periodic Benefit-Risk Evaluation Report) regulates the periodic submission of drug safety evaluations by marketing authorisation holders (MAHs). (9)
- ICH E2D (Post-Approval Safety Data Management): ICH E2D (Post-Approval Safety Data Management) supports post-marketing safety surveillance for marketed goods in India. (10)
- ICH E2E (Pharmacovigilance Planning): ICH E2E (Pharmacovigilance Planning) has an impact on Indian guidelines for risk management plans (RMPs) and pre- and post-authorization safety studies (PASS). (8)

3.3 Council for International Organisations of Medical Sciences (CIOMS)

The Council for International Organisations of Medical Sciences (CIOMS) has a significant impact on global pharmacovigilance (PV) policy, standards, and best practices. In order to address new concerns in risk management, clinical research, ethics, and pharmaceutical safety, CIOMS, which was founded in partnership with UNESCO and the WHO, creates recommendations based on consensus. CIOMS guidelines have a major influence on India because they bridge scientific, regulatory, and public health perspectives by offering flexible, evidence-based frameworks that complement WHO and ICH standards. (12)

CIOMS Working Groups' impact on India includes improved benefit-risk assessment and structured RMPs, patient and stakeholder involvement models, improved safety information provided by Indian pharmaceutical firms, Growing global acceptance of PvPI as a standardised PV system, Standardisation of ADR definitions and expedited reporting; enhanced signal detection methods; enhanced crisis response and risk communication. (13)

3.4 Global Guidelines for Biologics and Biosimilars

International frameworks such as the WHO recommendations on Biosimilar Evaluation, ICH Q5–Q12 quality and safety recommendations, and EMA/FDA biosimilar guidance have affected India's biologics PV system, which is a significant source of biosimilars.

Important factors affecting biologics and biosimilars include batch traceability, brand-name-specific reporting, immunogenicity monitoring requirements, vaccination and biologic post-marketing surveillance guidelines. (15)

3.5 European Medicines Agency (EMA) and FDA Guidelines

US Food and Drug Administration (FDA) Frameworks Applicable to India: (17)

- Indian MAHs' expectations for prompt reporting are impacted by Reporting Adverse Events After Marketing (21 CFR 314.80).
- Risk Evaluation and Mitigation Strategies (REMS) inform India's evolving approach to risk minimisation.
- FAERS (FDA Adverse Event Reporting System) serves as the model for transparent ADR databases and signal communication.

EU-GVP Components in India's Pharmacovigilance System: (19)

- **Module I, III and IV:** Pharmacovigilance Systems, Quality Systems and Audits
- **Module II:** Pharmacovigilance System Master File (PSMF)
- **Module V:** Risk Management Systems (RMS)
- **Module VI:** Individual Case Safety Report (ICSR) Processing and Reporting.
- **Module VII:** Periodic Safety Update Reports (PSURs) / Periodic Benefit-Risk Evaluation Reports (PBRERs)
- **Module IX:** Signal Management
- **Module X:** Additional Risk Minimization Measures (aRMMs)
- **Module XVI:** Safety Communication

4. Convergence of Indian PV with Global Standards

Harmonising India's pharmacovigilance (PV) framework with worldwide standards has been a primary strategic objective of the Pharmacovigilance Programme of India (PvPI) since its founding. As India developed into a global hub for medicines, particularly generics, vaccines, and biosimilars, it became crucial to align regulatory practices with international norms. Over the past ten years, India has made significant strides in terms of regulatory standards, reporting systems, data standards, and compliance criteria to guarantee that its PV ecosystem complies with worldwide safety surveillance methods. (13,15)

Compliance with ICH Regulations (E2 Series): An important milestone in India's harmonisation approach has been the incorporation of Council for harmonisation (ICH) E2 guidelines into national regulations. The CDSCO has progressively embraced the E2A–E2F concepts, which include quick reporting, frequent safety updates, risk management, and signal detection. India has established PSUR/PBRER rules, standardised SAE reporting schedules, and implemented organised risk-management planning for high-risk pharmaceuticals thanks to these adoptions. Additionally, for Indian pharmaceutical businesses doing business abroad, consistent standards across jurisdictions enhance regulatory certainty. (13,15)

The International Council for Harmonization's (ICH) E2 recommendations, which provide internationally recognised standards for drug safety reporting and monitoring, have gradually been adopted by the Pharmacovigilance Programme of India (PvPI), which is in charge of India's pharmacovigilance system. This alignment ensures that India's regulatory framework complies with international standards, improving both the quality of safety data and India's involvement in the global drug safety ecosystem. (19)

Case Safety Reports (ICSRs) are the foundation of pharmacovigilance. By following the ICH E2B(R3) standard for electronic reporting, India guarantees organised and compatible data input. Serious and unexpected adverse drug reactions (ADRs) are reported within globally defined timeframes, often fifteen days for major unexpected events, whereas fatal or life-threatening clinical trial events are recorded within seven days. Because of regulated coding using MedDRA nomenclature, which further ensures uniformity, Indian safety data may be easily linked into global databases like WHO VigiBase. (11,12)

Periodic Safety Update Reports (PSURs) and Periodic Benefit-Risk Evaluation Reports (PBRERs) provide periodic safety evaluation in accordance with ICH E2C(R2) guidelines. Indian regulations require worldwide data integration, benefit-risk assessment, and cumulative safety reporting. Subsequent reports must be submitted annually, while first reports must be made every six months. PBRERs ensure that India's submissions satisfy international standards by enabling the consistent evaluation of safety trends across jurisdictions for products sold abroad. India's growing adoption of ICH E2 standards has improved the quality and compatibility of ICSR globally. (11)

- Improved signal detection methods with empirical backing.
- Regular, consistent, and transparent safety reporting.
- Enhanced confidence from global regulatory organisations.
- Better public health protection thanks to standardised best practices.

Inclusion of CIOMS Suggestions: India's changing PV standards have been greatly influenced by the Council for International Organisations of Medical Sciences (CIOMS). Data quality, lifecycle-based safety evaluation, and consistent terminology usage have all improved because of India's adherence to CIOMS principles, including causality assessment (CIOMS I), harmonised case reporting (CIOMS II–III), and risk communication methods (CIOMS IV–VIII). Indian ICSRs are now more compatible with international databases like VigiBase and EudraVigilance thanks to these standardised procedures. (12, 13)

WHO Pharmacovigilance Standards Adoption: As an active participant in the WHO Programme for International Drug Monitoring, India has consistently modified its domestic practices to meet WHO global standards. This includes implementing crucial components for national PV centres, accepting the WHO-

UMC causality assessment technique, and standardising the use of MedDRA for categorising adverse events. active surveillance models, such as AEFI, AMR, and sentinel-site monitoring. (15)

To guarantee global harmonisation of safety monitoring, India's Pharmacovigilance Programme (PvPI), which is overseen by the Indian Pharmacopoeia Commission (IPC) under the jurisdiction of CDSCO, has methodically incorporated WHO-UMC global pharmacovigilance tools. Among these tools are:

- VigiBase is the worldwide WHO medication safety database: The Uppsala Monitoring Centre (UMC) in Sweden is in charge of it. The largest compilation of Individual Case Safety Reports (ICSRs) from over 130 countries globally. helps with global signal recognition, causality analysis, and regulatory decision-making. Gaining access to VigiBase is India's integration and role. In 2011, India became a full member of the WHO Programme for International Drug Monitoring (PIDM). PvPI continuously uploads the verified ADR data from ADR hotlines, national reporting portals, medical schools and hospitals, Centres for ADR Monitoring (AMCs), and Marketing Authorisation Holders, or MAHs. (20)
- VigiFlow is an online system for managing Individual Case Safety Reports (ICSRs). WHO-UMC provides its web-based ICSR management software. enables standardised pharmacovigilance processes such as quality control, MedDRA (Medical Dictionary for Regulatory Activities) coding, case input, and transfer to VigiBase. In India, PvPI adopted VigiFlow as its national pharmacovigilance database in 2011, replacing its earlier fragmented systems. Every ADR Monitoring Centre (AMC) in India uses VigiFlow to input ICSR data, do a narrative analysis, use MedDRA coding, perform automated quality inspections using WHO-UMC criteria, and submit reports to the National Coordination Centre (NCC). (20)
- VigiAccess is a public site providing information about international safety. (13,14)

Digital Convergence and Data Standardisation: Harmonisation has been facilitated by India's shift to internationally accepted digital PV standards. Important advancements consist of:

- XML-based reporting formats that facilitate easy electronic data input and are compatible with ICH E2B (R3).
- Individual case safety reports (ICSRs) are aligned with global E2B (R3) fields and terminologies. (11)
- Adoption of the WHO Drug and MedDRA drug dictionaries for drug classification and adverse event coding. (15)
- **Need for Digital Harmonization:** Problems with outdated systems (E2B R2): It has a strict data structure, restricted capacity to record complicated biologics and device data, insufficient fields for managing duplicates, and a lack of a universal transmission platform.

Objectives of digital harmonisation: (15,19)

Boost the completeness and quality of the data Make cross-regulator compatibility possible Encourage PV workflow automation Improve the identification of global signals Boost compatibility with WHO-UMC tools (VigiFlow, VigiBase, VigiLyze)

Regulatory mandate and gap analysis are followed by system upgrades, guideline formulation, training, pilot testing, gateway integration, complete implementation, and continuous optimisation in the E2B(R3) digital harmonisation pathway. Some of its advantages are standardised worldwide reporting, better data quality, enhanced real-time signal detection, smooth interface with WHO-UMC systems, and fewer manual errors. High technical and financial costs for MAHs, infrastructural deficiencies in developing areas, the difficulty of the R2 to R3 transition, the requirement for intensive training, and the possibility of data transmission errors during early adoption are all drawbacks. Digital Harmonisation Pathway: E2B(R3) Implementation Stages is displayed in **Table 1**. (19)

Table 1: Digital Harmonization Pathway: E2B(R3) Implementation Stages

S. No.	Stage	Description
1.	**Regulatory Mandate**	Announcement of regulatory deadlines, roadmap publication, and E2B(R3) acceptance.
2.	**Gap Analysis**	Evaluation of existing R2 systems, reporting procedures, and technical shortcomings in comparison to R3 specifications.
3.	**System Upgradation**	MedDRA version upgrades, database improvements, XML schema modifications, and validation rule integration.
4.	**Guideline Development**	Creation of gateway specifications, data-field definitions, and country submission regulations.
5.	**Stakeholder Training**	R3 capacity-building for IT teams, MAHs, AMCs, and medical facilities.
6.	**Pilot Testing**	ACK/NACK validation, error-resolution cycles, and controlled test submissions.
7.	**Gateway Integration**	Interoperability checks with international systems and integration with VigiFlow and VigiBase.
8.	**Full Implementation**	All ICSRs must use E2B (R3); submissions in R2 will no longer be accepted.
9.	**Monitoring & Optimization**	System improvements, ongoing quality checks, and schema upgrades in accordance with ICH guidelines.

a) **Convergence of Regulations for Clinical Trials:** Clinical trial safety regulations in India are becoming more in line with international standards, especially in:
- Accelerated serious adverse events reporting.
- Adoption of frameworks inspired by Good Pharmacovigilance Practices (GVP). (17)
- PSUR/PBRER submission harmonisation with ICH E2C (R2). (9)

b) **Enhancing Signal Detection and Risk Management:** The implementation of risk management plans (RMPs) in India that are in line with the EMA and ICH standards represents a significant advancement in international harmonisation. (19)
Increased ICSR number and quality, more dependable signal recognition and validation techniques, improved regulatory decision-making and integration into international PV networks, improved patient safety outcomes, and increased confidence from international regulators are all results of India's PV systems' compliance with international standards. [19]

In a number of sectors, CDSCO has successfully matched its regulatory framework with FDA and EMA requirements. GCP and clinical trial conduct, post-marketing safety and pharmacovigilance, GMP compliance and quality, CTD filing format, biologics and biosimilars regulations. Local modifications guarantee regulatory viability, public health relevance, and the concerns of patients in India. India's reputation in international drug development has grown because of this alignment, which has also made multinational trials and exports easier. CDSCO vs. EMA/FDA criteria are displayed in **Table 2** (13, 15,19)

Table 2: Mapping of CDSCO vs EMA/FDA guidelines

S. No.	Regulatory Area	CDSCO Guidelines (India)	EMA Guidelines (EU)	FDA Guidelines (US)	Notes / Local Adaptations
1.	**Good Manufacturing Practices (GMP)**	Based on the WHO GMP, risk-based inspections, documentation, and validation	EU GMP for APIs and finished products	cGMP (21 CFR Parts 210 & 211)	CDSCO incorporates multi-location inspections and Indian manufacturing realities
2.	**Clinical Trials (CT)**	GCP compliance; Ethics Committee approval; CTRI registration; protocol review; SAE reporting within 24 hours	EudraCT registration; EU Clinical Trials Regulation; GCP compliance	IND submission; FDA GCP; trial monitoring	Indian trials may require local bridging studies; timelines slightly adapted
3.	**Pharmacovigilance (PV)**	PvPI: AE reporting, PSURs, RMPs, signal detection	PSURs, RMPs, continuous PV	MedWatch, REMS, post-marketing safety monitoring	Indian ADR portal; toll-free reporting; local PV infrastructure
4.	**Drug Registration / CTD**	CTD format: Module 1 (regional), Modules 2–5 (quality, nonclinical, clinical)	e-CTD submission; modules 1–5	e-CTD submission; modules 1–5	Module 1 is India-specific; overall structure harmonized with ICH
5.	**Biologics / Biosimilars**	Guidelines on Similar Biologics (2012/2016); analytical & clinical comparability; PV plans	EMA biosimilar pathway; comparability exercise; clinical studies	351(k) biosimilar pathway; clinical equivalence; post-marketing surveillance	Local post-marketing PV infrastructure; optional bridging studies for the Indian population
	Regulatory Review & Approval	Science- and risk-based review;	EMA: scientific, risk-	FDA: Breakthrough	India-specific committees;

6.		accelerated approvals for critical drugs	based; PRIME accelerated pathway	Therapy, Priority Review	timelines adjusted for local capacity
7.	**Quality / Stability**	ICH Q1A–Q12 based stability & quality studies; DMF submissions	ICH Q1A–Q12 compliance	ICH Q1A–Q12 compliance	CDSCO may require stability data under Indian climatic zones (zone IV-b)
8.	**Ethics & Safety**	Ethics committee oversight; informed consent; GCP adherence	EU Clinical Trials Regulation; GCP	FDA 21 CFR Part 50/56; GCP	Indian ethical committees may review cultural/linguistic considerations

5. National Adaptations in Indian Pharmacovigilance

Although India's pharmacovigilance system under PvPI (Pharmacovigilance Programme of India) complies with ICH, EMA, and FDA standards, it includes a number of distinctive national modifications to accommodate regional healthcare, regulatory, and demographic circumstances. (14,15)

1. **Network of ADR Monitoring Centres (AMCs):** Unlike the FDA and EMA, which primarily rely on MAH and hospital reporting, India places a strong emphasis on direct healthcare professional reporting to enhance ADR capture in a variety of contexts. The country's extensive national network of AMCs includes private clinics, medical schools, and hospitals in both urban and rural areas. Local adaptation: Keep an eye on the incidence of diseases and drug use patterns in certain regions.
2. **Linguistic and Regional Customisation:** ADR reporting forms are available in a number of Indian languages to assist with language barriers. National PV guidelines guarantee inclusion by considering cultural considerations when gathering data and getting patient consent.
3. **Patient and Consumer Reporting Mechanisms:** Patients and consumers can report adverse drug reactions (ADRs) directly through PvPI by using online forms on the IPC website, toll-free lines, and the PvPI ADR reporting app on a mobile device. This method enhances patient-centric pharmacovigilance, in contrast to earlier methods where ADR reporting is mostly driven by experts. (14)
4. **Integration of VigiFlow with the National ADR Portal:** India uses VigiFlow to collect and send ICSRs to VigiBase in order to maintain global harmonisation. Special adaptation: By integrating with modules specific to India, including as AMCs, the PvPI app, and manual reporting procedures, the system is accessible across a variety of healthcare infrastructure levels. (20)
5. **Indian Context-Adapted Signal identification:** PvPI employs standard WHO-UMC signal identification methods. Special adaptation: prioritises signals for drugs that are commonly used in India, such as generic formulations, locally made vaccines or biologics, and traditional treatments (AYUSH), enables population-specific risk assessment that takes India's epidemiology and polypharmacy into account. (15)
6. **MAH Reporting Requirements with Indian Timelines:** MAHs in India are required to submit Periodic Safety Update Reports (PSURs), Risk Management Plans (RMPs), and ICSRs to PvPI. Localisation: PSURs that incorporate data on the Indian population, set deadlines (such a 15-day

reporting time for significant adverse drug reactions), and make regulatory decisions that consider the demographics of Indian patients. (14)

7. **Traditional Medicine Pharmacovigilance (Ayush): (14)**

- AYUSH (Ayurveda, Yoga & Naturopathy, Unani, Siddha, Homoeopathy) pharmacovigilance is a unique feature of PvPI.
- For traditional formulations, there are distinct reporting criteria, ADR monitoring centres, and safety review processes, which are uncommon worldwide.

8. **Post-Marketing Surveillance and Fast Alerts: (16)**

- PvPI actively uses CDSCO notifications to send out pharmaceutical security alerts and recalls.
- Fast reporting, including generic drugs, biosimilars, and vaccines, is adapted to the realities of the Indian market.
- Early detection and mitigation of safety issues in a vast, diversified population are ensured via adaptation tailored to India.

9. **Mobile Reporting and Digital Innovations: (15)**

- PvPI has created: ADR reporting app for mobile devices, an automated ADR capture through integration with hospital digital records, and instruments for decentralised, real-time reporting.
- India uses mobile-first tactics to reach rural and semi-urban communities, whereas EMA/FDA relies more on structured EHRs or MAH systems.

10. **Combining Programs for Public Health: (15)**

- ADR reporting is coordinated by PvPI with national immunisation programs, TB, malaria, HIV treatment programs, and other public health activities.
- This is a special adaptation that reflects India's healthcare delivery style and guarantees medication safety monitoring at the community level.

6. Challenges in Achieving Full Harmonization

1. Regulatory Alignment Challenges: CDSCO guidelines were not revised to reflect changes made by the FDA, ICH, and EMA. There is no coordination of country timetables for implementing new international PV standards. There is a lack of coordination between CDSCO, PvPI, IPC, MoHFW, and state agencies. There is still a lack of complete harmonisation between EU/FDA systems and reporting regulations like PSUR and RMP. (16)
2. Issues with Data Quality and Standardisation: Healthcare providers have substantially underreported, incomplete ICSRs with no laboratory data, follow-up information, or narratives, Data entry errors and inconsistent MedDRA coding AMCs differ in the calibre of their causality determinations. Seldom are standardised templates for SUSAR, ICSR, and PSUR/PBRER used. (15,19)
3. Gaps in Human Resources and Training: (15)

- Lack of clinical pharmacists and qualified PV specialists.
- Loss of continuity results from high personnel turnover in AMCs.
- Limited knowledge of vaccinations, medical devices, biologics, and biosimilars.
- Restricted development of advanced skills and inconsistent national training programs.

4. E2B (R3) Readiness & Digital Infrastructure: (10,11)

- AMCs, hospitals, and MAHs have different levels of IT capacity.
- Electronic health records (EHRs) and ADR reporting are not fully integrated.

- Inadequate capacity for gateway transmission and automated E2B(R3) XML.
- Electronic reporting is delayed in rural and semi-urban areas due to poor connectivity.
- Absence of national PV databases in real time that are comparable to FAERS and EudraVigilance.

5. Variability in Industry Compliance: (11)

- E2B (R3) compliance is a challenge for small and medium-sized pharmaceutical businesses.
- PSUR/PBRER entries vary in quality and completeness.
- Many businesses have inadequate PV quality management systems.
- Restricted practice of post-marketing research (PASS/PAES).

6. Issues with the Healthcare and Operational Systems: The time available for reporting adverse drug reactions (ADRs) is limited by the high patient loads in public hospitals. disparity between rural and urban areas' healthcare capacity, Regular clinical practice with insufficient documentation and limited PV integration are found in large private clinics and hospitals. Difficulties in Traditional Medicine PV and AYUSH. (14)

7. Awareness of Patients and Healthcare Workers regarding ADRs, clinicians' motivation is low because of their workload and lack of rewards, and Reporting is made more difficult by a variety of languages and literacy levels. (14)

8. Problems in the Monitoring of Advanced Therapies and Biologicals: Biologics and biosimilars have limited traceability (poor batch-level tracking). (14)

9. Limitations of Medical Device PV (Materiovigilance): (14)

- MvPI is being gradually scaled up throughout healthcare facilities.
- Limited knowledge of risk assessment and occurrences using devices.
- Lack of a reliable Unique Device Identification (UDI) system on par with FDA/EU standards.

10. Financial and resource constraints as well as legal, ethical, and governance concerns

11. Improper Development of Post-Marketing Evidence: (14)

- MAHs do PASS/PAES studies infrequently.
- Little cooperation between industry, academics, and regulatory agencies.
- India's real-world evidence (RWE) ecosystem is weak.

7. Opportunities and Future Directions

With increased involvement of stakeholders, regulatory coherence, and digital modernisation, India's pharmacovigilance system is set for significant improvement. The national implementation of E2B (R3), the incorporation of ADR reporting into EHRs, and the application of AI-based analytics for quicker signal detection are important prospects. Reporting quality will be improved by strengthening AMCs, increasing industry compliance, and improving patient interaction, particularly through mobile and multilingual solutions. Additional areas for expansion include coordinating AYUSH monitoring, increasing materiovigilance, and developing specialised expertise for biologics and advanced medicines. India can develop a fully integrated, cutting-edge, and globally resilient pharmacovigilance ecosystem with increased international cooperation and more rigorous policy frameworks. A table 3 has been incorporated showing opportunistic area and its future directions. Please refer to

Table *3* (14,15,16)

Table 3: Opportunities and Future Directions

S. No.	Opportunity Area	Future Directions
1.	**Digital Transformation**	Adoption of nationwide E2B (R3), incorporation of ADR reporting into EHR/e-prescription systems, real-time national PV dashboards, and AI/ML tools for predictive signal identification
2.	**Regulatory Harmonization**	Strengthened MAH PV quality systems; updated CDSCO guidelines and consolidated PV governance; complete compliance with ICH/EMA/FDA standards; and integrated drug-device-biologic vigilance
3.	**Strengthening AMC Network & Reporting**	Speciality AMCs (biologics, cancer, vaccines); Incentive-based ADR reporting; Multilingual patient reporting applications; Extension to district and private hospitals
4.	**Real-World Evidence (RWE)**	More PASS/PAES investigations; Connecting lab/prescription datasets with ADR data; National RWE platforms; Academic-regulator cooperation for RWE
5.	**AYUSH & Traditional Medicine PV**	Standardised AYUSH ADR instruments; databases on herbal safety; coordinated AYUSH–PvPI reporting; and enhanced causation frameworks
6.	**PV Workforce Development**	Academies for national training, Advanced training in biologics and vaccines; PV modules in medical, pharmacy, and AYUSH curricula; Development of device vigilance skills
7.	**Global Collaboration**	Increasing involvement in WHO-UMC and CIOMS; Contributing more to VigiBase; Establishing India as a global centre for PV analytics
8.	**Biologics, Biosimilars & Advanced Therapies**	Batch-level traceability; Gene/cell therapy safety guidelines; Long-term follow-up systems; Improved biosimilar PV frameworks
9.	**Medical Device Vigilance**	Post-market surveillance for high-risk and software-based devices; Expanded MvPI coverage; National UDI implementation
10.	**Policy, Governance & Ethics**	ADR reporting is required by law; Digital privacy laws are more rigorous; Unified national guidelines for the control of safety data

8. Conclusion

India has demonstrated its commitment to upholding international safety standards while retaining the flexibility necessary for its diverse healthcare environment by progressively harmonising its pharmacovigilance rules. Over the past ten years, India has upgraded PvPI operations, strengthened international cooperation, revised its laws and regulations, and adopted best practices from organisations like WHO, EMA, CIOMS, and ICH. However, full harmonisation is still a work in progress because of disparities in regulatory development, unequal reporting cultures, infrastructure limitations, and the therapeutic and demographic problems of the Indian population.

Despite these barriers, India has shown initiative by incorporating international recommendations with context-specific modifications, such as risk-based regulatory changes, enhanced biologics oversight, digital ADR platforms, and AYUSH pharmacovigilance. In the future, it will be crucial to make strategic investments in digital health infrastructure, capacity building, real-world evidence collection, artificial intelligence-based signal management, and more global-regional regulatory cooperation. India is well-positioned to develop into a globally significant, resilient, and patient-focused pharmacovigilance ecosystem by continuing to strike a balance between national demands and global convergence.

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