Project Title : Comparative Evaluation of Global ADR Reporting Systems & Signal Detection Approaches

Title Page

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1. Abstract

This project explores and compares adverse drug reaction (ADR) reporting systems and signal detection methodologies employed by global regulatory authorities, namely the WHO (VigiBase), US FDA (FAERS), and CDSCO (PvPI). By conducting a literature review, comparative analysis, and case studies, this self-initiated academic work simulates real-world pharmacovigilance workflows and regulatory expectations. It aims to demonstrate technical understanding of reporting formats, tools, data sources, and signal evaluation mechanisms. In addition, the report addresses global challenges, the role of MedDRA, and future innovations that shape the regulatory landscape.

2. Introduction

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems. With the increasing complexity of drug development and diverse patient populations, robust post-marketing surveillance is critical. International bodies like the WHO, FDA, and CDSCO have developed systems for ADR reporting and signal detection. This project aims to understand how these systems function and their effectiveness in real-world drug safety monitoring.

3. Objective

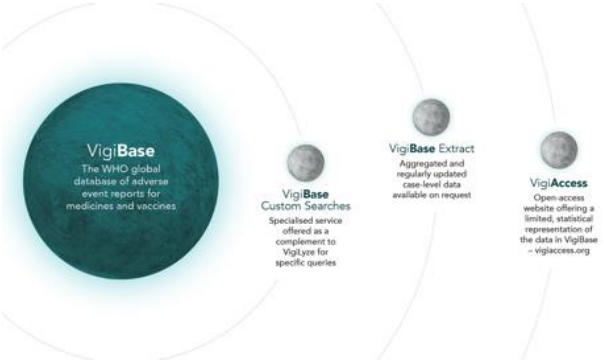
To analyze and compare ADR reporting systems and signal detection approaches used by WHO (VigiBase), US FDA (FAERS), and CDSCO (PvPI), while understanding their significance in ensuring patient safety. The project also seeks to highlight global challenges and future trends in pharmacovigilance.

4. Methodology

- Review of official regulatory websites and pharmacovigilance guidelines (WHO, FDA, CDSCO, ICH)
- Comparative tabular analysis of reporting systems and detection tools
- Case studies of significant drug withdrawals due to ADRs
- Analysis of MedDRA's role in harmonizing ADR classification
- Identification of emerging PV technologies (AI, Big Data)

5. Overview of Global PV Systems

WHO - VigiBase: A global database for Individual Case Safety Reports (ICSRs) managed by UMC. Contains over 25 million reports. Supports early signal identification using tools like VigiRank and VigiLyze.



US FDA - FAERS: The FDA Adverse Event Reporting System collects post-marketing ADR data from healthcare professionals, manufacturers, and consumers. Public access via FAERS dashboard.

CDSCO - PvPI: The Pharmacovigilance Programme of India, managed by IPC. Utilizes ADR reporting forms through AMCs. PvPI also collaborates with WHO.

6. Comparative Analysis of ADR Reporting

Parameter	WHO (VigiBase)	US FDA (FAERS)	CDSCO (PvPI)
Reporting Format	ICSR (CIOMS I)	MedWatch Form	PvPI ADR Form
Data Management Tool	VigiLyze	FAERS Dashboard	AMC Portal
Signal Detection Tool	VigiRank	Sentinel, FAERS	Manual Review
Reporting Frequency	Continuous	Quarterly	Monthly
Public Accessibility	Restricted	Open Access	Semi-public
Signal Prioritization	VigiGrade/VigiRank	PRR, ROR	Expert Panel
Causality Assessment Method	WHO-UMC Scale	Naranjo Scale	WHO-UMC Scale

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7. Signal Detection Methods

Quantitative Techniques:

- Disproportionality Analysis (PRR, ROR)
- Bayesian Confidence Propagation Neural Network (BCPNN)
- Empirical Bayes Geometric Mean (EBGM)

Qualitative Approaches:

- Case-by-case clinical review
- Literature scanning
- Regulatory agency alerts

ICH E2E Guidelines support integrating these methods into routine PV planning.

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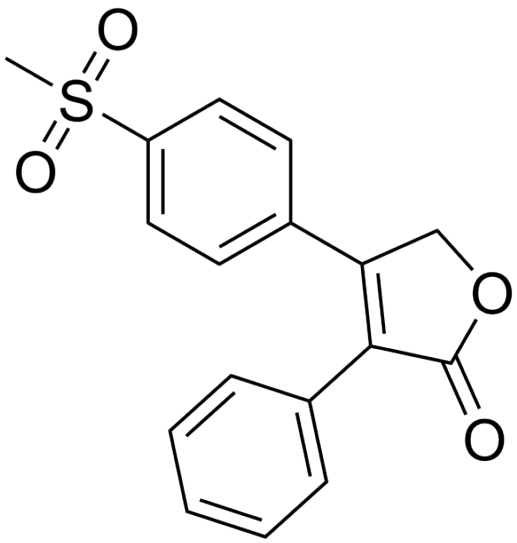
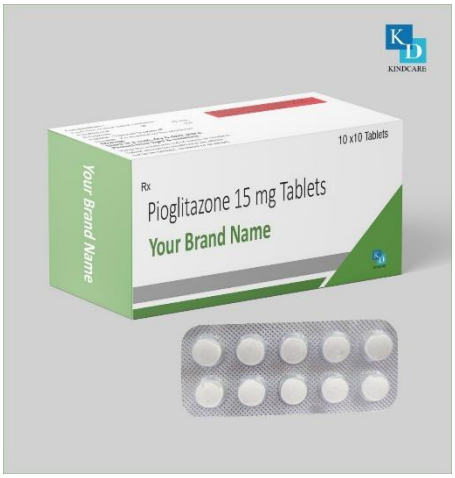
8. Case Study: Vioxx (Rofecoxib)

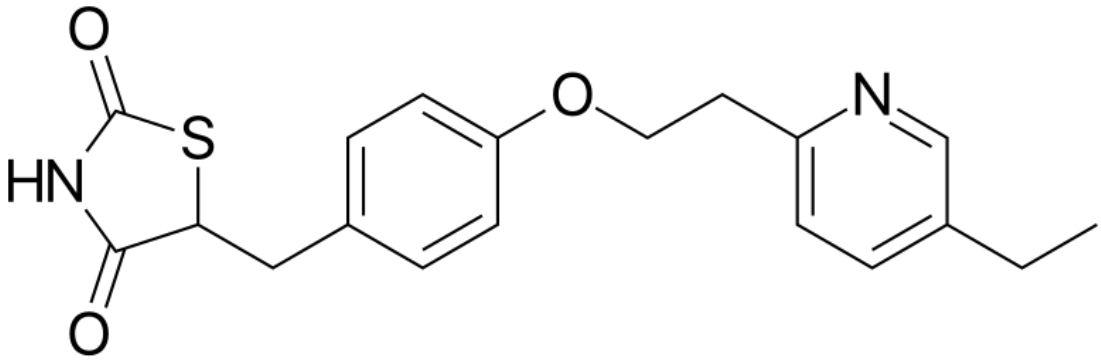
Rofecoxib was a selective COX-2 inhibitor marketed as Vioxx. Initially approved for osteoarthritis and pain, post-marketing surveillance linked it to increased cardiovascular events. In 2004, Merck withdrew the drug globally following the APPROVe study. The case underscored the role of signal detection, risk-benefit re-evaluation, and the ethical responsibility of MAHs.



9. Additional Case Analysis: Pioglitazone

Pioglitazone, an anti-diabetic drug, was linked with increased risk of bladder cancer in some studies. Regulatory actions included label warnings (US FDA) and temporary suspension (France, India). Reintroduction in India required enhanced PV measures. The case emphasizes regional regulatory divergence and post-marketing vigilance.





10. Key Findings & Discussion

- Global PV systems differ in tools, transparency, and data use.
- WHO emphasizes harmonized terminology and signal analytics.
- The FDA’s public dashboards offer transparency and robust data mining.
- India's PvPI faces limitations in digitization and public engagement.

11. Challenges in Global Pharmacovigilance

- Underreporting by healthcare providers
- Lack of awareness among patients
- Variability in causality assessments
- Differences in regulatory response to signals

12. Role of MedDRA and Standardization

MedDRA (Medical Dictionary for Regulatory Activities) standardizes terminology used in safety data. It enables:

- Cross-border signal sharing
- Accurate coding of adverse events
- Regulatory compliance and database interoperability

13. Future Trends in PV and Signal Detection

- Integration of Artificial Intelligence (AI) for early signal prediction
- Use of Real-World Evidence (RWE)
- Electronic Health Records (EHRs) for faster detection
- Mobile-based ADR reporting tools

14. Conclusion

This project has demonstrated the complexities and diversity in pharmacovigilance systems worldwide. It highlights the importance of harmonized practices, signal detection tools, case-based learning, and the increasing role of technology in drug safety. The acquired knowledge and analytical approach are strong assets for entry-level roles in regulatory affairs and pharmacovigilance.

15. References

- WHO Uppsala Monitoring Centre: https://www.who-umc.org
- US FDA FAERS: https://www.fda.gov
- CDSCO PvPI: https://www.ipc.gov.in
- ICH Guidelines: https://www.ich.org
- EMA GVP Modules: https://www.ema.europa.eu
- MedDRA MSSO: https://www.meddra.org
- Literature: PubMed, Google Scholar (for case studies)