APPLICATION OF MEDDRA IN SIGNAL DETECTION & RISK MANAGEMENT

Shifa Khan, Anchal Saroj, Krishnanand Prajapati

Nirmala Devi Pharmacy College, Jaunpur

Abstract

Pharmacovigilance is essential for ensuring drug safety by detecting, assessing, and preventing adverse drug reactions (ADRs) throughout the lifecycle of medicinal products. The Medical Dictionary for Regulatory Activities (MedDRA) serves as the global standard medical terminology that enables uniform coding and analysis of adverse event data across clinical trials, spontaneous reporting systems, and post-marketing surveillance databases. Its hierarchical structure, ranging from Lowest Level Terms (LLTs) to System Organ Classes (SOCs), facilitates consistent data standardization and improves the accuracy of signal detection methods such as data mining and disproportionality analysis in global databases like FAERS, EudraVigilance, and VigiBase. MedDRA also plays a key role in risk management processes, including risk management plans, risk minimization strategies, and continuous safety monitoring in clinical practice. Recent advancements in artificial intelligence, natural language processing, and real-world evidence integration are further enhancing MedDRA-based pharmacovigilance systems by enabling faster and more efficient detection of safety signals. Despite challenges such as coding variability, structural complexity, and implementation issues, MedDRA remains a cornerstone of modern pharmacovigilance, significantly contributing to global drug safety assessment and regulatory decision-making.

Keywords: *MedDRA, pharmacovigilance, signal detection, risk management, adverse drug reactions (ADRs)*

Corresponding Author

Shifa Khan

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1. INTRODUCTION

A crucial field in contemporary medicine, pharmacovigilance focuses on the identification, evaluation, comprehension, and avoidance of side effects or other drug-related issues. Ensuring medication safety has become a top public health issue due to the growing complexity of therapeutic agents and the increase in drug use worldwide. In order to protect patients and maximize the benefit-risk ratio of pharmaceuticals across the course of their lifecycle, effective pharmacovigilance systems are crucial (World Health Organization [WHO], 2002; Edwards & Aronson, 2000).

The inconsistent reporting and interpretation of adverse medication events is one of the main issues in pharmacovigilance. Accurate signal detection and risk assessment can be severely hampered by terminology variability, contradictory clinical descriptions, and variations in coding techniques between nations and databases. Standardized medical terminologies are necessary to overcome this problem by harmonizing data collection and analysis on a global scale (Hauben & Aronson, 2007; Bate & Evans, 2009).

In order to facilitate pharmacovigilance and regulatory communication, the Medical Dictionary for Regulatory Activities (MedDRA) was created as a globally standardized medical terminology. Clinical researchers, pharmaceutical companies, and regulatory bodies all frequently utilize it to code adverse events in clinical trials and post-marketing surveillance systems. Both thorough and aggregated analysis of safety data is made possible by MedDRA's highly organized hierarchical system, which ranges from extremely specific Lowest Level Terms (LLTs) to wide System Organ Classes (SOCs) (ICH, 2023; Brown et al., 1999).

By facilitating uniform adverse event classification across sizable pharmacovigilance databases like FAERS, EudraVigilance, and VigiBase, MedDRA plays a crucial role in signal discovery. This standardization strengthens the capacity to recognize uncommon or newly emerging adverse medication reactions and increases the dependability of statistical techniques used to find possible safety alerts. Additionally, by guaranteeing consistent interpretation and distribution of safety information across international regulatory systems, MedDRA promotes regulatory risk management initiatives (EMA, 2024; Norén et al., 2013).

The significance of MedDRA in pharmacovigilance has increased recently because to developments in data mining, artificial intelligence, and the creation of real-world evidence. To reliably and efficiently handle massive amounts of safety data, these systems rely on standardized and structured vocabulary. Because of this, MedDRA is now a crucial component of contemporary digital pharmacovigilance systems designed to enhance patient safety and regulatory decision-making (Harpaz et al., 2020; Liu et al., 2019).

The application of MedDRA in signal detection and risk management is the main topic of this review paper, which also highlights its structure, function in pharmacovigilance systems, contribution to data mining methods, and new developments in AI-driven safety monitoring. The difficulties and potential outcomes of implementing MedDRA in international healthcare systems are also discussed.

2. MedDRA: Structure and Coding System

A internationally standardized clinical terminology called MedDRA (Medical Dictionary for Regulatory Activities) was created to facilitate the classification, retrieval, and analysis of adverse event data in pharmacovigilance and regulatory procedures. It improves the quality and consistency of safety data analysis by enabling consistent interpretation of medical data across clinical trials, post-marketing surveillance, and regulatory filings (Brown et al., 1999; ICH, 2023).

2.1 Hierarchical structure of MedDRA (SOC to LLT)

The five-level hierarchical structure of the MedDRA nomenclature is intended to enable both extremely specific and wide coding of medical concepts. At the highest level, broad categories based on anatomical, physiological, or etiological systems—such as gastrointestinal or cardiac disorders—are represented by System Organ Class (SOC). SOCs are crucial for aggregate safety signal interpretation and offer a macro-level framework for arranging adverse event data (Brown et al., 1999; ICH, 2023).

High Level Group Terms (HLGT) and High Level Terms (HLT), which further refine medical concepts into intermediate categories, are located beneath SOC. HLTs gather medically related Preferred Terms, while HLGTs cluster related HLTs. This mid-level hierarchy enables meaningful aggregation of safety signals across related clinical situations and permits organized categorization of adverse events for regulatory analysis (MedDRA MSSO, 2025; Brown et al., 1999).

Preferred Terms (PTs), like "nausea" or "hypertension," are single, unique medical concepts utilized in regulatory reporting at the most detailed level. One or more Lowest Level Terms (LLTs), such as synonyms, colloquial language, spelling variations, and clinically similar terms reported in everyday situations, are associated with each PT (e.g., "stomach upset" mapped to "dyspepsia"). (ICH, 2023; Edwards & Aronson, 2000).

Reliable data gathering, signal detection, and regulatory decision-making are made possible by this hierarchical framework, which guarantees that disparate clinical terminologies are standardized into uniform medical concepts. Additionally, MedDRA is very flexible for pharmacovigilance applications, supporting both comprehensive case-level analysis at the PT/LLT level and wide epidemiological assessments at the SOC level (FDA, 2019; Bate & Evans, 2009).

Table 1: Hierarchical Structure of MedDRA

MedDRA Level	Description	Example	Purpose in Pharmacovigilance
System Organ Class (SOC)	Broadest level grouping by organ/system	Nervous system disorders	High-level safety signal analysis
High Level Group Term (HLGT)	Group of related HLTs	Central nervous system disorders NEC	Intermediate aggregation
High Level Term (HLT)	Group of related PTs	Headaches NEC	Pattern identification
Preferred Term (PT)	Standardized medical concept	Headache	Primary analysis unit in signal detection
Lowest Level Term (LLT)	Most detailed term (verbatim report)	Severe throbbing headache	

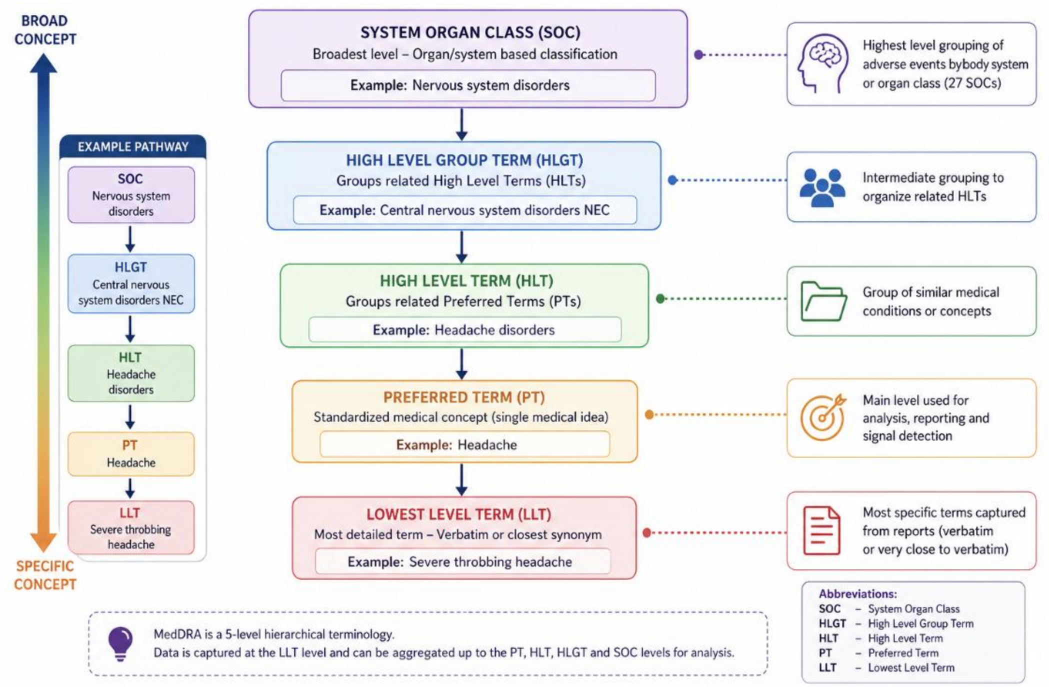

Figure 1: MedDRA Hierarchical Structure

2.2 Coding principles and terminology selection

The standardized procedure known as MedDRA coding ensures uniformity in pharmacovigilance databases across the globe by translating verbatim clinical reports of adverse events into controlled terminology. The quality of safety signal detection, regulatory reporting, and benefit-risk assessment of pharmaceuticals are all directly impacted by coding accuracy (Brown et al., 1999; Hauben & Bate, 2009).

Verbatim-to-LLT mapping, which matches the reported term to the most appropriate Lowest Level Term (LLT) without changing the original clinical meaning, is a fundamental component of MedDRA coding. In order to prevent interpretation bias, coders are trained to choose the closest medically relevant LLT, which is thereafter automatically associated with a Preferred Term (PT) for analysis (ICH, 2023; Ghosh et al., 2017).

In order to ensure alignment with established MedDRA terms, terminology is chosen using a context-preserving technique, which preserves as much of the original reporter's wording as feasible. This is especially crucial in systems for spontaneous reporting, because descriptions could be vague, insufficient, or of varying quality. Standardization preserves the reported event's clinical value while reducing ambiguity (Alves et al., 2015).

phrase specificity selection, in which coders select the most precise phrase based on available clinical information, is another crucial component. For example, where context allows, general phrases like "infection" are clarified into more precise LLTs like "urinary tract infection." As a result, signal detection algorithms have better data granularity (Blake et al., 2010).

The MedDRA Maintenance and Support Services Organization (MSSO), which offers frequent updates, term selection guidelines, and standardized coding processes to reduce inter-coder variability, supports MedDRA's incorporation of coding consistency norms and conventions. These rules provide uniformity among pharmaceutical businesses and regulatory bodies worldwide (MedDRA MSSO, 2025).

Furthermore, multilingual and multinational pharmacovigilance reporting is supported by MedDRA coding, which enables the mapping of terminology from several languages and healthcare systems into a single structure. This is crucial for international safety databases that gather information from many regulatory areas (Curtis et al., 2018).

In general, adverse event data is consistently organized for reliable pharmacovigilance analysis and regulatory evaluation according to the MedDRA coding rules, which place an emphasis on correctness, repeatability, and clinical neutrality.

2.3 Version control and maintenance by MSSO

MedDRA is a constantly changing terminology system that needs to be updated on a regular basis to stay up to speed with new adverse event reports, developments in medical science, and changing legal requirements. The Medical Dictionary for Regulatory Activities Maintenance and Support Services Organization (MSSO) is in charge of updating, maintaining, and disseminating MedDRA versions throughout the world, guaranteeing both regulatory uniformity and scientific relevance (MSSO, 2025).

MedDRA's version control is updated twice a year, usually in March and September. New terms are added, old terms are modified, and out-of-date or inappropriate terms are removed or deactivated as part of these changes. While preserving backward compatibility for historical data analysis, this structured update method guarantees that MedDRA reflects current clinical knowledge (ICH, 2023; Smalley et al., 2016).

The change request mechanism, which allows users like pharmaceutical companies, regulatory bodies, and healthcare institutions to suggest new terms or revisions, is a crucial part of MedDRA maintenance. Before being approved, every request is subjected to a thorough scientific evaluation by MSSO medical specialists to guarantee compliance with MedDRA's hierarchical structure and coding principles (Harpaz et al., 2012).

Through established validation procedures including synonym management, hierarchical consistency checks, and cross-referencing with current medical ontologies, MSSO also guarantees quality control and terminological integrity. According to Brown et al. (1999) and Hauben & Bate (2009), this avoids duplication and guarantees logical connections between terms across System Organ Classes (SOC), High Level Terms (HLT), and Preferred Terms (PT).

Impact analysis of changes, which enables users to comprehend how updates may influence previously coded safety data, is another crucial component of version control. This is crucial for pharmacovigilance since changes in mapping or re-coding can affect regulatory reporting trends and signal detection results (MedDRA MSSO, 2025).

To guarantee correct deployment of updates across international pharmacovigilance systems, MSSO also offers comprehensive user assistance and training tools, such as term selection guidelines, maintenance manuals, and workshops. This makes it easier for regulatory bodies like the FDA, EMA, and PMDA to harmonize (Curtis et al., 2018).

All things considered, MSSO's organized version control and maintenance framework guarantees that MedDRA will continue to be a dynamic, globally harmonized, and scientifically sound terminology system that is necessary for precise pharmacovigilance and drug safety monitoring.

3. Role of MedDRA in Pharmacovigilance

By offering a consistent and internationally recognized nomenclature for the categorization, reporting, and analysis of adverse events, MedDRA plays a crucial role in contemporary pharmacovigilance. Consistent interpretation of safety data across nations, healthcare systems, and regulatory bodies is made possible by its organized vocabulary. For medication safety assessments to be reliable and comparable across the product lifecycle, this standardization is crucial (ICH, 2023; Banerjee et al., 2018).

3.1 Standardization of adverse event reporting

One of MedDRA's most important contributions to pharmacovigilance is the standardization of adverse event (AE) reporting. Adverse occurrences are frequently described using non-uniform, colloquial, or institution-specific vocabulary in clinical practice and spontaneous reporting systems. In order to enable consistent data aggregation and analysis, MedDRA transforms a variety of clinical phrases into uniformly coded terms (Brown et al., 1999; Hauben et al., 2017).

MedDRA makes guarantee that similar or identical medical concepts are consistently recorded in safety databases by mapping verbatim reported phrases to standardized Lowest Level phrases (LLTs) and then to Preferred Terms (PTs). For instance, a single PT can standardize terms like "stomach upset," "gastric discomfort," and "dyspepsia," enabling precise assessment of event frequency and pattern identification (Edwards & Aronson, 2000; MedDRA MSSO, 2025).

In regulatory systems like the FDA Adverse Event Reporting System (FAERS), EudraVigilance, and WHO VigiBase, where large-scale datasets need consistent nomenclature for effective analysis, this harmonization greatly improves the quality of pharmacovigilance data. Duplication, misclassification, and underreporting of safety signals would greatly rise in the absence of such standardization (Curtis et al., 2018; Alomar, 2014).

By enabling pharmaceutical businesses and regulatory bodies to exchange adverse event data using a standard medical language, MedDRA also promotes worldwide regulatory harmonization. In multi-regional clinical trials and post-marketing surveillance, where data from various populations must be merged for safety evaluation, this is especially crucial (Banerjee et al., 2018).

Additionally, by guaranteeing that input data are consistent and comparable across datasets, standardized reporting enhances the efficacy of signal identification algorithms, including disproportionality studies like Proportional Reporting Ratio (PRR) and Reporting Odds Ratio (ROR). In the end, this reduces noise from inconsistent terminology usage while strengthening the recognition of genuine safety signals (Hauben & Bate, 2009; Poluzzi et al., 2012).

All things considered, the foundation of trustworthy pharmacovigilance systems is MedDRA-driven uniformity of adverse event reporting, which facilitates precise signal detection, regulatory decision-making, and enhanced patient safety globally.

3.2 Integration with global safety databases (FAERS, EudraVigilance, VigiBase)

Adverse drug response (ADR) data may be collected, exchanged, and analyzed uniformly across regulatory countries thanks to MedDRA, a core coding standard for large international pharmacovigilance databases. Its incorporation into international safety systems guarantees that diverse reports from various healthcare environments are transformed into a single terminology framework, enabling effective worldwide signal detection and regulatory decision-making (ICH, 2023; EMA, 2024).

MedDRA is used by the FDA Adverse Event Reporting System (FAERS), one of the biggest spontaneous reporting databases in the world, to code adverse event terminology supplied by manufacturers, consumers, and healthcare providers. In order to find possible safety signals connected to medications that are marketed in the US, FAERS data can be methodically examined using statistical and data mining techniques thanks to standardized MedDRA coding (FDA, 2022; Banda et al., 2016).

Similar to this, MedDRA is the required language for reporting potential adverse reactions within the European Union through the EudraVigilance system of the European Medicines Agency. Effective case aggregation at various levels (PT, HLT, SOC) is made possible by the structured MedDRA hierarchy, which also facilitates quick transmission of safety concerns across EU member states and supports regulatory assessment of new hazards (EMA, 2024; Moore et al., 2014).

Globally, safety records from more than 140 nations are integrated by the WHO Programme for International Drug Monitoring via its VigiBase. For multilingual and international data submissions to be consistent, MedDRA is essential. Because of this harmonization, the Uppsala Monitoring Centre (UMC) is able to discover unusual or geographically distributed adverse drug responses that might not be found in separate national databases and conduct large-scale signal detection (Uppsala Monitoring Centre, 2023; Lindquist, 2008).

Collaborative pharmacovigilance amongst organizations like the FDA, EMA, and WHO is made possible by the integration of MedDRA across various databases, which also facilitates interoperability and cross-regulatory data interchange. According to Banerjee et al. (2018), this worldwide alignment increases the effectiveness of risk assessment, decreases effort duplication, and improves early detection of drug safety issues globally.

Additionally, because consistent coding lowers noise and increases the dependability of statistical outputs like disproportionality assessments, the usage of a similar vocabulary improves the efficacy of automated signal recognition algorithms. In big databases like FAERS and VigiBase, where millions of complaints are analyzed for safety surveillance, this is especially crucial (Hauben & Aronson, 2007).

All things considered, the foundation of contemporary pharmacovigilance infrastructure is MedDRA's integration into worldwide safety databases, which permits consistent reporting, effective regulatory communication, and thorough international drug safety monitoring.

3.3 Importance in regulatory reporting systems

By offering a worldwide standardized nomenclature that guarantees uniformity, precision, and effectiveness in the submission and assessment of adverse event data, MedDRA plays a crucial role in regulatory reporting systems. In order to evaluate the benefit-risk profile of pharmaceuticals, regulatory bodies need standardized safety reports. MedDRA makes this possible by transforming various clinical narratives into organized, interpretable data (ICH, 2023; EMA, 2024).

Supporting International Council for Harmonization (ICH) E2B rules, which specify the electronic delivery of individual case safety reports (ICSRs), is one of MedDRA's main benefits in regulatory reporting. MedDRA-coded data reduces disparities in safety review by ensuring that adverse event information given by pharmaceutical companies is understood consistently across regulatory bodies like the FDA, EMA, and PMDA (ICH, 2016; Kubota et al., 2019).

MedDRA also enhances the quality and comparability of regulatory submissions by enabling structured aggregation of adverse events at different hierarchical levels (PT, HLT, SOC). This enhances the identification of new risks during post-marketing surveillance and clinical trial monitoring by enabling regulators to examine both particular clinical occurrences and more general safety patterns (Brown et al., 1999; Moore et al., 2014).

Additionally, by making safety data evaluations more understandable, MedDRA facilitates effective signal evaluation and decision-making procedures. To find trends, evaluate causality, and decide whether regulatory measures like label modifications, warnings, or drug withdrawals are required, regulatory assessors rely on standardized coding. Variability in nomenclature would seriously impede regulatory interpretation in the absence of such standardization (Hauben & Aronson, 2007; Sarayani et al., 2018).

MedDRA serves as a common language that facilitates communication between multinational regulatory bodies, which is another significant feature of its role in global regulatory convergence. Because safety data must be exchanged across several regulatory jurisdictions without losing meaning or interpretability, this harmonization is especially crucial for multinational clinical trials and international pharmacovigilance initiatives (Banerjee et al., 2018).

Additionally, MedDRA increases the effectiveness of regulatory reporting through data mining compatibility and automation. Because of its structured nature, it may be integrated with pharmacovigilance software systems to automate signal detection, case processing, and the creation of periodic safety update reports (PSURs). As a result, regulatory decision-making proceeds more quickly and with less human labor (Alves et al., 2015).

All things considered, MedDRA is a crucial part of contemporary regulatory reporting systems, guaranteeing that adverse event data is internationally interpretable, consistently structured, and appropriate for thorough safety assessment and regulatory action.

4. MedDRA in Signal Detection

Because it offers a consistent medical language for classifying adverse events across clinical trials, spontaneous reporting systems, and actual healthcare databases, MedDRA is a key component of pharmacovigilance signal identification. MedDRA allows for the systematic identification, comparison, and statistical evaluation of drug-event interactions across vast diverse datasets by translating free-text clinical descriptions into standardized Preferred Terms (PTs) (Hauben & Aronson, 2007; ICH, 2023).

The capacity of MedDRA to provide multi-level data analysis, where safety information may be evaluated at several hierarchical levels (LLT, PT, HLT, SOC), is a significant advantage in signal detection. This adaptability increases the sensitivity of pharmacovigilance systems by enabling regulators and researchers to identify both individual clinical concerns and more general safety patterns (Bate & Evans, 2009; Curtis et al., 2018).

4.1 Concept of safety signal in pharmacovigilance

Information from one or more sources that points to a possible new or established link between a pharmaceutical product and an adverse event that needs more investigation is referred to as a safety signal. Crucially, a signal acts as an early warning indicator that prompts further research rather than confirming causality (WHO, 2002; Edwards et al., 2010).

A statistically odd or clinically unexpected pattern of adverse event reporting linked to a medication is typically used to identify safety signals. These signals could come from observational databases, clinical research, or spontaneous reporting systems. By guaranteeing that adverse occurrences are coded consistently, lowering variability, and enhancing the dependability of signal detection outputs, MedDRA improves this procedure (Hauben & Bate, 2009; Hauben et al., 2017).

Depending on the degree of evidence and evaluation, signals are really classified as prospective signals, validated signals, or confirmed dangers. Before taking any risk management action, signals are subjected to a systematic evaluation process that includes clinical examination, epidemiological validation, and regulatory assessment (Edwards et al., 2010; EMA, 2024).

4.2 Data mining and signal detection methods using MedDRA

In pharmacovigilance, data mining entails using statistical, computational, and algorithmic methods to find hidden or new safety patterns in sizable adverse event databases. Because it guarantees that adverse events are consistently recorded and comparable across datasets, MedDRA-coded data is crucial for these techniques (Harpaz et al., 2013; Norén et al., 2013).

Frequency-based analysis is a common method that looks for anomalous increases in the number of reports for a certain MedDRA Preferred Term over time. Trend analysis is another popular technique that tracks changes in reporting patterns over time or among various populations in order to identify new risks early on (Bate & Evans, 2009).

Automated signal detection algorithms, which continuously search sizable databases like FAERS, EudraVigilance, and VigiBase, are another feature of contemporary pharmacovigilance systems. According to Curtis et al. (2018) and Banda et al. (2016), these systems mainly rely on MedDRA coding to guarantee that input data is standardized, allowing for precise statistical association computation and lowering noise from inconsistent terminology.

Furthermore, MedDRA-relevant phrases are being extracted from unstructured clinical narratives like electronic health records and case reports using text mining and natural language processing (NLP) approaches. This raises the sensitivity of signal detection systems and greatly increases data capturing efficiency (Wang et al., 2017).

4.3 Disproportionality analysis (PRR, ROR, IC methods)

One of the most popular quantitative techniques for identifying safety alerts in databases with MedDRA codes is disproportionality analysis. In comparison to all other drug-event combinations in the database, it evaluates if a particular drug-adverse event combination occurs more frequently than anticipated (Evans et al., 2001; Rothman et al., 2004).

The proportion of a particular adverse event for a medication is compared to the proportion of the same occurrence for all other medications using the Proportional Reporting Ratio (PRR). A greater PRR indicates a possible safety alert that has to be investigated further. Similar to this, the Reporting Odds Ratio (ROR), a measure of disproportionality frequently employed in regulatory evaluations, assesses the likelihood of reporting a certain occurrence with a medicine compared to all other pharmaceuticals (Evans et al., 2001; Poluzzi et al., 2012).

By minimizing extreme values and false-positive results in huge datasets, Bayesian techniques like the Information Component (IC) used in WHO's VigiBase and the Empirical Bayes Geometric Mean (EBGM) used in FDA systems enhance signal detection. For uncommon adverse occurrences, where conventional frequency-based methods could be less dependable, these techniques are very helpful (Norén et al., 2013; Hauben & Bate, 2009).The adoption of standardized MedDRA Preferred Terms, which guarantees that related clinical concepts are classified consistently, is a crucial prerequisite for all of these approaches. Because different publications use different wording, statistical comparisons would not be trustworthy without MedDRA standardization (Bate & Evans, 2009).

Table 2: Comparison of Signal Detection Methods Using MedDRA

Method	Type	Key Measure	Strengths	Limitations
PRR (Proportional Reporting Ratio)	Frequentist	Ratio of reporting proportions	Simple, easy to interpret	Less reliable for rare events
ROR (Reporting Odds Ratio)	Frequentist	Odds of event reporting	Widely used in regulatory systems	Sensitive to reporting bias
IC (Information Component)	Bayesian	Log likelihood ratio	Reduces noise, better for rare ADRs	Complex interpretation
EBGM (Empirical Bayes Geometric Mean)	Bayesian	Shrinkage estimator	Reduces false positives	Computationally intensive

4.4 Identification of adverse drug reactions (ADRs)

By facilitating the systematic categorization of documented clinical events, MedDRA plays a crucial part in the detection and assessment of adverse drug reactions (ADRs). Identifying adverse drug reactions (ADRs) entails separating actual medication-related effects from comorbidities, background disease symptoms, or coincidental events (Edwards & Aronson, 2000; Alomar, 2014).

Pharmacovigilance systems can aggregate similar adverse event reports across populations and spot trends that might not be apparent at the individual case level by standardizing adverse event descriptions into MedDRA words. In real-world situations, this is especially crucial for identifying uncommon, delayed, or severe adverse drug reactions (ADRs) that might only manifest with extensive drug exposure (Hauben et al., 2017; Sarayani et al., 2018).

Additionally, MedDRA facilitates signal validation and refinement, in which statistical signals that were first identified are evaluated using epidemiological data, biological plausibility, and clinical judgment. This stage guarantees that regulatory bodies only verify and address clinically significant adverse drug reactions (ADRs) (Edwards et al., 2010; EMA, 2024).

Additionally, MedDRA-coded ADR data helps regulators determine if a drug's therapeutic advantages outweigh its dangers through benefit-risk evaluation. Decisions like label revisions, restricted use, or market withdrawal require this procedure (ICH, 2023; Moore et al., 2014).

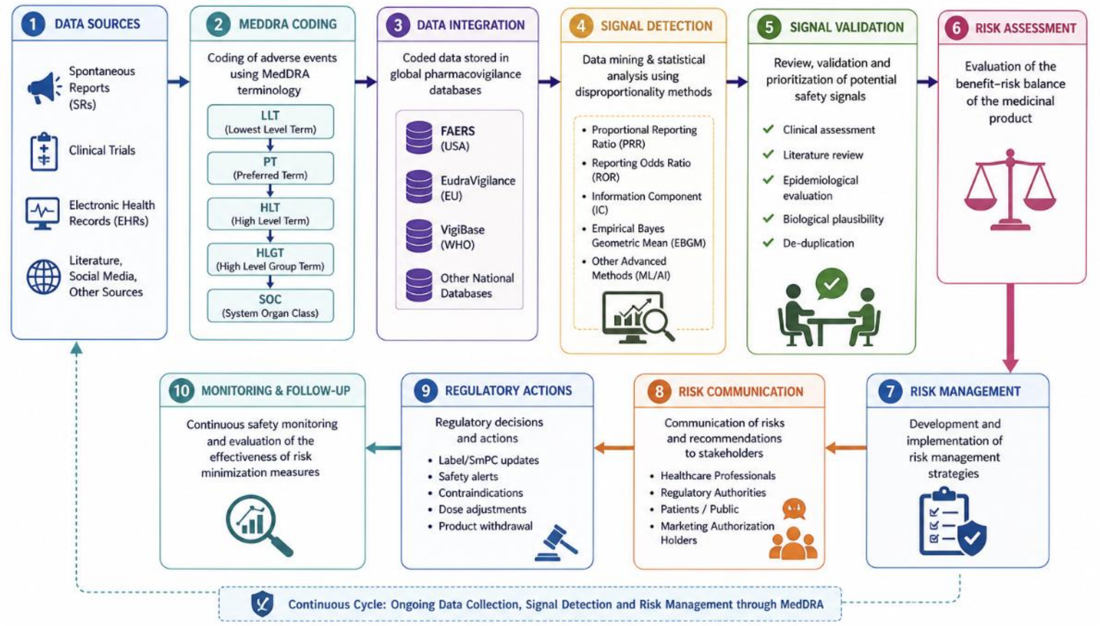

Figure 2: Signal Detection and Risk Management Workflow Using MedDRA

5. MedDRA in Risk Management

In pharmacovigilance, risk management is the methodical process of determining, assessing, reducing, and disseminating the risks connected to pharmaceuticals during the course of their lifecycle. By offering a defined nomenclature that guarantees uniform classification of safety data, MedDRA plays a critical role in this process, facilitating efficient risk assessment and regulatory decision-making (ICH, 2023; EMA, 2024).

5.1 Risk management plans (RMPs) and their components

A systematic regulatory document called a Risk Management Plan (RMP) is necessary for pharmaceuticals to guarantee that the advantages of their use outweigh the dangers. RMPs specify how risks will be recognized, described, avoided, or reduced, as well as how these actions' efficacy will be tracked over time (EMA, 2024; Santoro et al., 2017).

The safety specification, pharmacovigilance strategy, and risk minimization plan are the essential elements of an RMP. The pharmacovigilance strategy outlines procedures for continuous safety monitoring, whereas the safety specification uses clinical trial and post-marketing data to identify known and prospective concerns. Strategies to lessen the probability or severity of adverse responses in clinical practice are part of the risk minimization plan (EU GVP Module V, 2023; Banerjee et al., 2018).

By guaranteeing that all safety issues are classified uniformly, MedDRA facilitates the establishment of RMPs by enabling producers and regulators to methodically assess and contrast risk profiles across various products and populations (ICH, 2023).

5.2 Role of MedDRA in risk identification and evaluation

By standardizing adverse event data from many sources, including as clinical trials, spontaneous reports, and observational studies, MedDRA plays a crucial role in the discovery and assessment of drug-related risks. Safety data may be accurately aggregated and compared across international datasets thanks to this standardization (Hauben et al., 2017; Curtis et al., 2018).

By classifying identical adverse events under Preferred Terms (PTs) and higher-level classifications like High Level Terms (HLTs) and System Organ Classes (SOCs), MedDRA-coded data facilitates the identification of growing safety concerns during risk identification. Regulators can detect system-wide and specific risks related to pharmaceuticals with the aid of this hierarchical framework (Bate & Evans, 2009).

By offering uniform nomenclature for assessing the frequency, severity, and clinical significance of adverse events, MedDRA makes organized benefit-risk assessment in risk appraisal easier. This enables regulatory bodies to evaluate the acceptability of detected risks in light of therapeutic advantages (Sarayani et al., 2018; EMA, 2024).

5.3 Risk minimization strategies in clinical practice

Once risks have been recognized and assessed, risk minimization techniques seek to lessen the frequency or severity of adverse medication reactions. These tactics could be standard (e.g., package inserts and labeling revisions) or extra (e.g., patient monitoring requirements, educational materials, or restricted access programs) (EU GVP Module XVI, 2023; Banerjee et al., 2018).

By guaranteeing that safety information conveyed in product labels, correspondence with healthcare professionals, and regulatory papers is founded on standardized vocabulary, MedDRA supports these tactics. As a result, risks are communicated to patients and doctors more clearly and consistently (ICH, 2023).

Additionally, by analyzing changes in adverse event reporting trends over time, MedDRA-coded data enables regulators to assess the efficacy of risk mitigation strategies. Successful application of risk mitigation techniques may be shown by a decrease in particular MedDRA-coded events (Curtis et al., 2018).

5.4 Post-marketing surveillance and safety monitoring

In order to identify uncommon, delayed, or long-term adverse medication reactions that might not be seen during clinical trials, post-marketing surveillance, or PMS, is crucial. Electronic health records, registry data, and spontaneous adverse event reports are all coded and analyzed using MedDRA in PMS systems (WHO, 2002; Hauben & Aronson, 2007). MedDRA coding is used by international pharmacovigilance databases as FAERS, EudraVigilance, and VigiBase to provide consistent data integration and analysis. This makes it possible to continuously evaluate medication safety profiles and makes it easier to identify new concerns in various groups and geographical areas (EMA, 2024; Lindquist, 2008).

By guaranteeing that adverse event data is standardized, MedDRA also improves the efficacy of signal detection systems used in post-marketing surveillance, increasing the precision of statistical studies and trend assessments. According to Bate & Evans (2009) and Norén et al. (2013), this facilitates prompt regulatory actions like label modifications, safety alerts, or market withdrawal when required.

Overall, MedDRA is indispensable in post-marketing safety monitoring, as it ensures that real-world safety data is consistently structured, globally comparable, and suitable for ongoing risk evaluation.

6. Challenges and Limitations

Despite being the worldwide standard for medical terminology in pharmacovigilance and regulatory reporting, MedDRA has a number of practical drawbacks. These difficulties are mostly caused by human-dependent coding, structural complexity, interpretation heterogeneity, and problems with integration across international safety systems. If not appropriately handled, these constraints may affect the precision of signal identification, risk assessment, and regulatory decision-making (Brown et al., 1999; Hauben & Aronson, 2007).

6.1 Coding variability and term ambiguity

Coding variability, which occurs when different coders assign different MedDRA terms to the same adverse event description, is a significant difficulty in MedDRA implementation. In spontaneous reporting systems, where clinical narratives are frequently fragmentary, subjective, or non-standardized, this inter-coder discrepancy is more prevalent. The homogeneity of pharmacovigilance datasets may be impacted as a result of comparable cases being coded under various Lowest Level Terms (LLTs) or Preferred Terms (PTs) (Alves et al., 2015; Ghosh et al., 2017).

Coding accuracy is further complicated by term ambiguity. Numerous reported symptoms, such "weakness," "fatigue," or "pain," are non-specific and may be interpreted differently based on the clinical setting. Coders may choose more general or imprecise terms in the absence of adequate clinical information, which lowers the granularity of safety data and may dilute genuine safety signals during analysis (Edwards & Aronson, 2000; Banerjee et al., 2018).

In addition, subjective interpretation of clinical narratives can introduce **human bias**, which may affect consistency across different organizations or countries. This remains a persistent challenge in global pharmacovigilance systems where multiple stakeholders contribute to safety reporting (Hauben et al., 2017).

6.2 Complexity of hierarchical structure

Despite its great flexibility, MedDRA's hierarchical structure makes processing and interpreting data much more difficult. It can be difficult for novice users to comprehend the relationships between various levels of aggregation in the five-level hierarchy (LLT, PT, HLT, HLGT, and SOC) (ICH, 2023; Curtis et al., 2018).Another level of complication is introduced by MedDRA's multi-axial design, which allows a single Preferred Term to be connected to several System Organ Classes. While this increases the flexibility of data retrieval, improper use of primary SOC assignment rules may result in duplication or inconsistent grouping of safety data (Bate & Evans, 2009).

The accuracy of pharmacovigilance analysis can also be impacted by improper term aggregation or disaggregation, which can either obscure crucial safety signals (over-aggregation) or provide false signals (over-segmentation) (Norén et al., 2013).

6.3 Data inconsistency and aggregation issues

Data inconsistency is still a major drawback for MedDRA-based systems, even with global standards. Data quality in databases like FAERS, EudraVigilance, and VigiBase might vary depending on national differences in reporting culture, healthcare infrastructure, and regulatory standards (Lindquist, 2008; Curtis et al., 2018).

Inconsistent aggregate of adverse events is another problem, as minor phrasing variations may cause equivalent clinical situations to be recorded under various PTs. In uncommon bad events in particular, this can fragment data and lower the statistical strength of signal identification techniques (Harpaz et al., 2013).

On the other hand, clinically significant information may be obscured by excessive aggregation at higher hierarchical levels (like SOC). One of the main drawbacks of MedDRA-based pharmacovigilance analysis is the trade-off between sensitivity and specificity (Poluzzi et al., 2012; Norén et al., 2013).

Additionally, variations in database structure and coding practices between regulatory agencies can limit **cross-database comparability**, even though MedDRA provides a common terminology framework (Banerjee et al., 2018).

6.4 Training and implementation challenges

It takes specific training and ongoing skill development to utilize MedDRA effectively. However, inconsistent coding procedures are sometimes caused by differences in training quality among organizations, particularly among new pharmacovigilance experts. Data dependability and quality in safety assessments may be directly impacted by this (MedDRA MSSO, 2025; Alves et al., 2015).

The difficult learning curve involved in comprehending MedDRA hierarchy, coding norms, and term selection criteria is another significant drawback. Insufficient training could result in users choosing terms inaccurately, which could distort safety signals and misclassify adverse occurrences (Ghosh et al., 2017).It can be difficult to integrate MedDRA into current pharmacovigilance systems and electronic health record (EHR) platforms from an operational standpoint. Variations in database design, mapping tools, and software architecture frequently necessitate substantial technical adaptation, which raises implementation time and expense (Wang et al., 2017).

Additionally, there are continuous maintenance issues due to the frequent MedDRA updates (twice a year). Periodically re-coding or re-mapping historical data is necessary since each update may include new terms, change current ones, or deactivate out-of-date terms. For regulatory bodies and pharmaceutical corporations, this may need a lot of resources (ICH, 2023; MedDRA MSSO, 2025).

7. Future Perspectives

The development of data science, artificial intelligence (AI), and practical healthcare analytics is closely linked to the future of MedDRA in pharmacovigilance. Intelligent technologies that improve the speed, accuracy, and sensitivity of signal detection and risk management are rapidly being added to traditional human and semi-automated approaches as worldwide safety databases continue to expand in size and complexity (Bate et al., 2020; EMA, 2024).

7.1 Artificial intelligence in MedDRA-based signal detection

By enabling automated examination of extensive MedDRA-coded datasets, artificial intelligence and machine learning are revolutionizing pharmacovigilance. Complex, non-linear correlations between medications and adverse events that can be difficult to find with conventional disproportionality techniques can be found using AI systems. By continuously learning from updated safety data, these systems enhance early signal detection (Liu et al., 2019; Harpaz et al., 2020).

By directly mapping unstructured clinical narratives to standardized MedDRA terminology, natural language processing (NLP) tools significantly improve MedDRA utility. This increases consistency in the classification of adverse events and lessens the workload associated with manual coding. In order to decrease coding variability and increase term mapping accuracy, deep learning algorithms are also being investigated (Wang et al., 2017; Shang et al., 2021).

In addition, AI-based systems can prioritize safety signals based on clinical relevance, severity, and historical patterns, thereby supporting regulatory decision-making and improving pharmacovigilance efficiency (Bate et al., 2020).

7.2 Integration of real-world evidence (RWE)

In pharmacovigilance, real-world evidence (RWE) integration is becoming more and more crucial. Electronic health records (EHRs), insurance claims, patient registries, and wearable technology are examples of real-world data sources from which RWE is obtained. The standardized framework needed to unify adverse event data taken from these many sources is provided by MedDRA (Sherman et al., 2016; EMA, 2024).

By mapping real-world clinical data to MedDRA terms, researchers can perform large-scale observational studies to assess long-term drug safety and effectiveness. This enhances the ability to detect rare or delayed adverse drug reactions that may not be captured during clinical trials (Corrigan-Curay et al., 2018).

Furthermore, RWE combined with MedDRA-coded data enables **continuous benefit–risk assessment**, allowing regulatory authorities to update safety profiles dynamically as new evidence emerges (Makady et al., 2017).

7.3 Automation and digital pharmacovigilance systems

Modern pharmacovigilance systems are undergoing a revolution thanks to automation. MedDRA coding is now integrated with signal detection algorithms, automated case processing, and regulatory reporting workflows on sophisticated digital systems. As a result, adverse event evaluation is completed more quickly and accurately while requiring less human labor (Alves et al., 2015; EMA, 2024).

Robotic process automation (RPA) is increasingly used to handle repetitive pharmacovigilance tasks such as case intake, data cleaning, and MedDRA coding suggestions. These systems enhance efficiency while reducing human error in large-scale safety databases (Bate et al., 2020).

Pharmaceutical businesses and regulatory authorities can exchange real-time data through cloud-based pharmacovigilance solutions. This guarantees quicker identification of safety signals across various regions and enhances international cooperation (Curtis et al., 2018).

Overall, automation and digital transformation are expected to make MedDRA-based pharmacovigilance systems more proactive, predictive, and globally integrated in the coming years.

8. Conclusion

MedDRA has established itself as an essential global standard for medical terminology in pharmacovigilance, playing a central role in ensuring consistency, accuracy, and harmonization of adverse event reporting across clinical trials, post-marketing surveillance, and regulatory databases. Its structured hierarchical framework enables efficient coding of clinical information, which supports reliable data analysis, signal detection, and risk assessment at both granular and aggregated levels.

In signal detection, MedDRA significantly enhances the ability to identify potential safety concerns by standardizing adverse event terminology across large and diverse datasets. This standardization improves the performance of statistical methods such as disproportionality analysis and facilitates early detection of emerging drug safety issues. As a result, regulatory authorities and pharmaceutical industries can respond more effectively to potential risks, ensuring timely interventions and improved patient safety.

In risk management, MedDRA supports structured evaluation and communication of safety information, contributing to the development of risk management plans, risk minimization strategies, and post-marketing surveillance activities. Its integration with global pharmacovigilance systems such as FAERS, EudraVigilance, and VigiBase further strengthens international collaboration and regulatory harmonization.

Despite its advantages, challenges such as coding variability, structural complexity, and implementation issues persist, highlighting the need for continuous training, improved automation, and advanced technological integration. The future of MedDRA is expected to be shaped by artificial intelligence, real-world evidence, and digital pharmacovigilance systems, which will further enhance its efficiency and predictive capability.

Overall, MedDRA remains a critical pillar of modern pharmacovigilance, enabling robust drug safety monitoring and supporting evidence-based regulatory decision-making to protect public health globally.

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10. Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this review.

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