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REVIEW ARTICLE ON ADVERSE EVENT AND CASE PROCESSING IN PHARMACOVIGILANCE

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ABSTRACT

In pharmacovigilance the valid case consisting an identifiable reporter, identifiable patient, suspected product, adverse event, if any one of them is missing then it considered to be invalid case in Case processing. Pharmacovigilance (PV) Means detecting, assessing, understanding, and preventing adverse effects or any other drug-related problems. It plays a Major role in ensuring the ongoing safety of medicinal products after they enter the market. The core of PV activities involves monitoring adverse events (AEs) and conducting efficient case processing to ensure patient safety and regulatory compliance.

Pharmacovigilance plays a pivotal role in ensuring the safety and effectiveness of medicinal products by systematically identifying, assessing, and preventing adverse drug reactions (ADRs). Adverse event (AE) reporting and case processing form the backbone of post-marketing surveillance, enabling early detection of safety signals. The process typically involves the collection of AE data from diverse sources such as healthcare professionals, patients, literature, and regulatory databases, followed by case validation, coding using standardized terminologies like MedDRA[6], causality assessment, and expedited reporting to regulatory authorities. Efficient case processing ensures data accuracy, regulatory compliance, and timely communication of potential risks. Technological advancements, including automation, artificial intelligence, and real-world evidence platforms, are increasingly enhancing the quality and speed of pharmacovigilance activities. This article explores the critical components of AE reporting and case processing, highlights current challenges such as underreporting and data quality, and discusses evolving trends to strengthen global drug safety systems.

KEY WORDS: *Adverse Event, Spontaneous reporting, ICSR (Individual Case Safety Report), Duplicate check, MeDRa, causality assessment, Narrative writing.*

1. INTRODUCTION

Pharmacovigilance plays a critical role in ensuring the safety, efficacy, and risk management of medicinal products throughout their lifecycle [(1)]. An essential component of this discipline is the identification, documentation, and evaluation of **adverse events (AEs)**—any unfavorable medical occurrence experienced by a patient following the use of a pharmaceutical product, regardless of whether a causal relationship is established [(2)]. Monitoring these events allows healthcare systems and regulatory authorities to detect potential safety signals and prevent harm to patients[(3)].

Case processing is the structured methodology used to manage adverse event reports. It involves the collection, verification, assessment, coding, and documentation of AE cases received from various sources, including clinical trials, post-marketing surveillance, literature, and spontaneous reporting systems. Accurate and timely case processing ensures compliance with global regulatory standards and enables the detection of trends that may signal emerging safety concerns [(4)].

With the increasing volume of real-world data and stringent regulatory expectations, effective adverse event case processing has become central to maintaining public health, enhancing drug safety profiles, and guiding evidence-based decision-making. Continuous improvements in reporting systems, technology integration, and standardized workflows are transforming pharmacovigilance into a more proactive and data-driven discipline [(5).]

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2. UNDERSTANDING ADVERSE EVENTS

An adverse event (AE) is any undesirable medical occurrence in a patient taking a pharmaceutical product, which does not necessarily have a causal relationship with the treatment.

Adverse Event vs Adverse Drug Reaction (ADR)

Term	Definition	Causality Required?
Adverse Event (AE)	Any negative medical occurrence after drug use	❌ No
Adverse Drug Reaction (ADR)	Harmful effect directly caused by the drug	✅ Yes

So, **every ADR is an AE, but not every AE is an ADR**

1. Adverse Event Occurs
2. AE Report is Collected
   - Patient
   - Healthcare Professional
   - Literature / Studies
   - Regulatory Databases
3. Case Intake & Logging
   - Enter into safety database
   - Assign case ID
4. Case Validation

   Check for 4 minimum criteria:

   ✓ Identifiable reporter
   ✓ Identifiable patient
   ✓ Suspect drug/substance
   ✓ Adverse event description
5. Data Coding (e.g., MedDRA terms)
6. Causality Assessment
   - Evaluate relationship between AE and the suspected product
7. Medical Review
   - Clinical safety team reviews accuracy
   - Add narrative and seriousness status
8. Reporting Decision
   - Expedited (15-day / 7-day reports)
   - Periodic safety update reports (PSUR/PBRER)
9. Regulatory Submission
10. Follow-up & Case Closure
    - Request missing info
    - Finalize outcome in database

3. UNDERSTANDING CASE PROCESSING

Case processing is a structured workflow used to handle reports of adverse events related to medicinal products. It ensures that each reported case is accurately documented, assessed, and submitted to regulatory authorities within mandated timelines. The process begins with **case intake**, where data is received from sources such as healthcare professionals, patients, clinical trials, literature, or spontaneous reports. A valid case must include four essential elements: an identifiable patient, a reporter, a suspect product, and an adverse event [5].

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Case Intake

↓

Validity Check (Patient + Reporter + Drug + Event?)

↓

Valid Case? → No → Archive / Follow-up

↓ Yes

Case Registration (Unique Case ID)

↓

Data Entry & MedDRA/WHO-DD Coding

↓

Causality Assessment

↓

Seriousness & Expectedness Assessment

↓

Regulatory Reporting Decision

↓

Quality Control (QC) Review

↓

Reporting to Authorities

↓

Case Closure & Archiving

Once the case is received, it goes through **data entry and verification**, followed by **medical coding** using standardized dictionaries like MedDRA. **Causality assessment** [(1)] is then performed to evaluate the likelihood that the drug caused the event. Next, the case is **prioritized**, classified (e.g., serious or non-serious), and checked for **regulatory reporting requirements**, such as timelines for expedited submissions.

Finally, the case is **quality-reviewed**, finalized, and submitted electronically to authorities via systems like EudraVigilance or FDA's FAERS. Proper case processing not only ensures compliance but also contributes to signal detection and overall drug safety monitoring. Challenges such as incomplete data, underreporting, and workload volume make accuracy, timeliness, and process efficiency essential [(9)].

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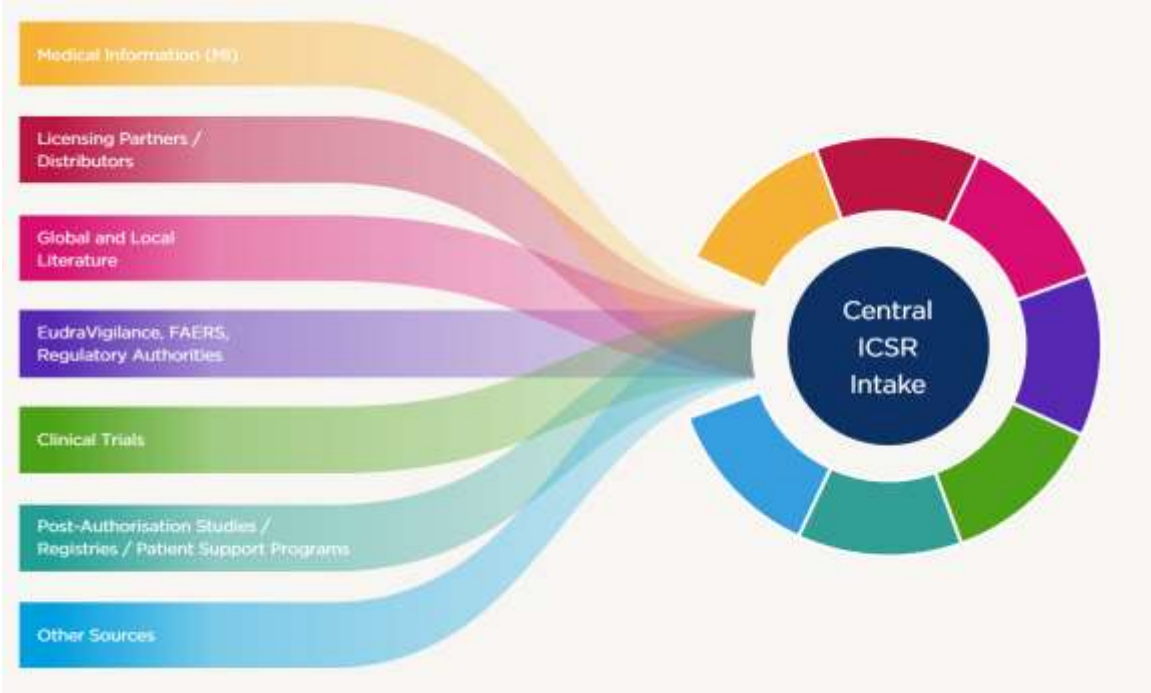

Fig. no. 1 central ICSR intake in pharmacovigilance from Primevigilance group

4. NEED OF WORK

Why Adverse Event Reporting and Case Processing Are Essential in Pharmacovigilance?

1. Ensuring Patient Safety

- The primary goal of pharmacovigilance is to detect, assess, and prevent harm caused by medicines.
- Prompt reporting and processing of AEs help identify unknown or serious reactions early.
- It reduces risk to patients using the same or related drugs.

2. Regulatory Compliance

- Health authorities like the FDA, EMA, and CDSCO require timely reporting of adverse events.
- Companies must follow strict timelines (e.g., 7-day or 15-day expedited reports).
- Proper case processing ensures adherence to Good Pharmacovigilance Practices (GVP) and avoids penalties.

3. Continuous Benefit–Risk Assessment

- AE data helps evaluate if the benefits of a drug still outweigh its risks.
- Signals from processed cases lead to:
  - Label updates
  - Safety warnings
  - Product recalls (if needed)

4. Detection of Safety Signals

- Case processing allows aggregation and analysis of reports from different regions.
- It helps identify patterns, rare adverse reactions, or previously unknown risks.

5. Improving Drug Development

- Post-marketing AE data supports drug lifecycle management.
- Information from case processing helps modify formulations or dosing recommendations.

6. Building Public and Physician Trust

- Transparent monitoring of adverse events builds confidence in medicines.
- Healthcare providers rely on updated safety information for prescribing decisions.

7. Legal and Ethical Responsibility

- Companies are ethically bound to monitor product safety post-approval.
- Failure in AE case processing could lead to litigation or loss of credibility.

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8. Supports Risk Management Plans (RMP)

- Processed AE data is used to update risk minimization strategies.
- Helps in creating educational materials for doctors and patients.

➢ **Summary in One Line:**

Adverse event handling and case processing are critical to protect patients, meet legal obligations, detect safety signals, and maintain the overall benefit–risk balance of medicines.

5. TYPES OF ADVERSE EVENTS

- **Serious AEs (SAEs)**
  An AE is considered serious if it results in:
  - ➢ Death
  - ➢ Life-threatening condition
  - ➢ Hospitalization (initial or prolonged)
  - ➢ Disability or incapacity
  - ➢ Congenital anomaly
  - ➢ Requires intervention to prevent serious outcome
- **Non-Serious AEs**
  Mild to moderate events that do not result in severe outcomes.
- **Adverse Drug Reactions (ADRs)**
  Adverse events where a causal link to a drug is established.

a) Dose-Related (Type A)

➢ Predictable and based on drug's pharmacology
Example: Hypotension from antihypertensives

b) Non–Dose-Related (Type B)

➢ Unpredictable, uncommon, often immune-related
Example: Stevens-Johnson syndrome

c) Chronic (Type C)

➢ Due to long-term use
Example: Steroid-induced osteoporosis

d) Delayed (Type D)

➢ Appear after some time
Example: Carcinogenic effects

e) Withdrawal (Type E)

➢ After discontinuation
Example: Opioid withdrawal symptoms

6. SOURCES OF AE REPORTS

- Healthcare professionals
- Patients/consumers
- Clinical trials
- Literature
- Social media
- Regulatory authorities

7. CASE PROCESSING IN PHARMACOVIGILANCE

Case processing involves capturing, evaluating, and reporting AE cases according to regulatory standards. Each case must contain four minimum criteria:

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- Identifiable patient
- Identifiable reporter
- Suspect drug
- Adverse event

Key Steps in Case Processing

1. Data Collection and Intake
   - Receipt of the report via phone, email, apps, literature, or spontaneous reports.
   - Initial logging and verification.

2. Data Entry and Validation
   - Entry into safety databases like Argus, ARISg, or Veeva Vault.
   - Validation of completeness and accuracy.
   - Assessment for seriousness and expectedness.

3. Medical Assessment
   - Performed by trained medical reviewers.
   - Causality assessment (e.g., WHO-UMC, Naranjo algorithm).
   - Identification of key clinical information and outcomes.

4. Coding
   - Adverse events coded using MedDRA terminology.
   - Drugs coded via WHO Drug Dictionary or INN names.

5. Narrative Writing
   - Clear, medico-scientific narrative summarizing the case.
   - Reflects patient history, treatment details, AE description, and outcomes.
6. Quality Review
   - Reconciliation and QC checks to ensure compliance.
   - Correction of inconsistencies.

7. Regulatory Reporting
   - Submission timelines:
     - 15 days for serious unexpected cases.
     - 90 days for non-serious cases.
   - Reporting via systems such as **EudraVigilance**, FDA (FAERS), MHRA, or local authorities.

10. IMPORTANCE OF AE CASE PROCESSING IN PHARMACOVIGILANCE

AE case processing is the **core function** of pharmacovigilance and plays a vital role in ensuring patient safety, regulatory compliance, and drug lifecycle management. Its importance can be understood through the following key points

1. Ensures Patient Safety

- Identifies potential risks and unexpected reactions early
- Helps prevent harm by issuing safety alerts, warnings, or label updates
- Protects vulnerable populations like children, elderly, or pregnant women

2. Detects Safety Signals and Trends

- Aggregated AE data reveals patterns of drug-related harm
- Supports proactive risk minimization and corrective actions
- Enables health authorities to issue recalls or restrictions when needed

3. Supports Regulatory Compliance

- Mandatory reporting to agencies (e.g., FDA, EMA, CDSCO, MHRA)
- Ensures adherence to strict reporting timelines (7-day/15-day/periodic reports)

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4. Improves Benefit–Risk Assessment
- Balances therapeutic value against potential hazards
- Helps healthcare professionals make safer prescribing decisions
- Supports drug label updates or dosage modifications

5. Enhances Public Health Outcomes
- Reduces morbidity and mortality caused by unsafe drug reactions
- Builds public trust in healthcare and pharmaceuticals
- Enables policy development and surveillance programs

6. Contributes to Scientific Research and Knowledge
- Generates real-world data beyond clinical trials
- Helps understand rare, long-term, or population-specific reactions
- Informs future drug development and safety monitoring strategies

7. Supports Market Authorization and Post-Marketing Surveillance
- Ensures continuous monitoring after approval
- Helps maintain regulatory approval and market access
- Facilitates renewal and compliance audits

8. Prevents Litigation and Financial Risks
- Early detection and action reduce chances of lawsuits
- Protects pharmaceutical companies from financial losses and recalls

11. CHALLENGES IN AE CASE PROCESSING

Incomplete or Poor-Quality Data
- Missing patient details, drug information, or event description
- Lack of follow-up from reporters
- Difficulty in validating causality

Underreporting of Adverse Events
- Patients and healthcare professionals may not report mild or moderate cases
- Cultural, legal, and awareness barriers
- Fear of legal consequences or lack of time

High Case Volume
- Increasing reports due to global drug use, digital submissions, and regulations
- Difficulties in prioritizing serious events over non-serious ones

Regulatory Compliance Pressure
- Strict and varying reporting timelines (e.g., 7-day and 15-day expedited reports)
- Constant updates in global regulations (EMA, FDA, CDSCO, MHRA, etc.)
- Risk of penalties for non-compliance

Data Standardization Issues
- Multiple data formats from different sources (E2B, literature, call centers, apps)
- Coding difficulties using MedDRA or WHO-DD
- Risk of misclassification and duplication

Resource and Workforce Limitations
- Need for trained PV professionals
- Workload imbalance and burnout
- High cost of maintaining large PV teams

Global Language and Regional Barriers
- Reports in different languages
- Regional terminologies and translation issues

Signal Detection Complexity

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- Difficulty in identifying true safety signals vs noise
- Managing false positives or delayed recognition

Technology Integration Challenges

- Transition from manual entry to automated systems
- Issues with compatibility, validation, and cybersecurity
- AI/ML adoption barriers

Follow-up and Case Closure Delays

- Difficulty obtaining additional data from reporters
- Long timelines for clarifications
- Impact on case completeness and reporting deadlines

12. TECHNOLOGICAL ADVANCEMENTS

Modern PV uses:

- AI and NLP tools for case triage
- Automation in data entry
- Signal detection software
- Integrated safety databases
- EHR and mobile app reporting

13. SAFETY REPORT OF CASE PROCESSING ON HYPOTHETICAL DRUG- VIGILANT

A formal safety report in case processing is called an **Individual Case Safety Report (ICSR)**. It is a standardized document that captures all the data regarding a single patient's adverse event (AE) experience.

➢ **Simulated Individual Case Safety Report (ICSR)**

Field	Detail
Safety Database ID	PV-2025-04-0123
Report Type	Spontaneous (Consumer)
Regulatory Clock Start Date	2025-10-10
Seriousness	Serious (Requires Inpatient Hospitalization)
Source Type	Initial Report

1) Patient Information (Anonymized)

Field	Detail
Patient Initials	Pandurang
Age/Sex	60-year-old Male
Weight	80 kg
Relevant Medical History	Type 2 Diabetes Mellitus, Mild Hypertension (controlled)

2) Suspect Drug Information

Field	Detail
Suspect Drug Name	**Drug-Vigilant** (Active Ingredient: Hypotensil-Z)
Indication for Use	High Blood Pressure (Hypertension)
Daily Dose	10 mg, once daily (QD)
Route	Oral
Therapy Start Date	2025-09-01
Therapy Stop Date	2025-10-10 (Discontinued due to AE)

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3) Adverse Event (AE) Details

Field	Detail
Reported Event	Severe Dizziness and Fainting (Syncope)
MedDRA Code (PT)	Syncope (Preferred Term)
Onset Date	2025-10-09
Event Seriousness Criteria	Required Inpatient Hospitalization
Dechallenge/Rechallenge	Dechallenge: Positive (Event resolved after stopping drug)
Event Outcome	Recovered

4) PV Assessment and Conclusion

Field	Detail
Causality Assessment (Sponsor)	**Probable/Likely.** The syncopal episode occurred shortly after initiation of a new anti-hypertensive drug (known to cause orthostatic hypotension), and the event rapidly resolved upon drug withdrawal (positive dechallenge).
Expectedness Assessment	**Unexpected.** The prescribing information (Company Core Data Sheet) lists "dizziness" as a known event, but does **not** list "Syncope" requiring hospitalization.
Regulatory Action	Expedited (15-day) reporting to all relevant Health Authorities required due to seriousness and unexpectedness.

5) Pharmacovigilance Narrative (The Story of the Case)

Source: Initial report received via telephone from the patient's wife (Consumer) on 2025-10-10.

A 68-year-old male with a medical history of Type 2 Diabetes and controlled Hypertension started taking **Drug-Vigilant 10 mg QD** on **2025-09-01** for the treatment of high blood pressure. On **2025-10-09**, after 38 days of therapy, the patient experienced a sudden episode of **severe dizziness** followed by **fainting (syncope)** while getting out of bed. The fall resulted in a minor head abrasion. Emergency medical services (EMS) were called, and the patient was transported to the local hospital. The treating physician admitted the patient overnight for observation and evaluation of the syncopal episode. A review of the patient's records indicated his blood pressure was significantly lower than usual upon admission. **Drug-Vigilant was discontinued** on **2025-10-10** in the hospital. The patient reported complete resolution of dizziness and had no further syncopal episodes prior to discharge on 2025-10-11. The reporter confirmed no other new or concomitant medications were started during the month of therapy.

13. RESULT

The research highlights that **Adverse Event (AE) case processing is the core function of pharmacovigilance**, playing a critical role in drug safety throughout a product's lifecycle.

1. The Case Processing Workflow (The Backbone of PV)

Case processing is a structured workflow for handling AE reports to ensure regulatory compliance and timely signal detection. The process is highly standardized:

- **Minimum Criteria for a Valid Case:** An AE report must contain four essential elements to be considered valid: an **identifiable patient**, an **identifiable reporter**, a **suspect drug**, and an **adverse event description**.
- **Key Steps:** The workflow includes **Case Intake** (receiving the report), **Validation** (checking the four minimum criteria), **Data Entry & Coding** (using standardized terms like **MedDRA** for events and **WHO-DD** for drugs), **Causality Assessment**, **Medical Review**, **Regulatory Reporting Decision** (e.g., 7-day or 15-day expedited reports), and **Quality Control**.
- **Output:** The formal safety report generated by this process is the **Individual Case Safety Report (ICSR)**, which captures all data regarding a single patient's AE experience.

2. Importance of AE Case Processing

The necessity of this process stems from multiple critical objectives

- **Patient Safety:** The primary goal is to promptly detect unknown or serious reactions, identify potential risks, and issue safety alerts to prevent patient harm.

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- **Regulatory Compliance:** It ensures mandatory and timely reporting to health authorities (like the FDA, EMA, and CDSCO) and adherence to strict reporting timelines, which is crucial to avoid legal penalties and maintain market authorization.
- **Signal Detection and Risk Assessment:** Aggregated AE data from processed cases helps detect safety signals, evaluate the **benefit–risk balance** of medicines, and guides corrective actions like label updates, safety warnings, or product recalls.

3. Key Challenges and Technological Advancements

The effectiveness of PV is hampered by several challenges:

- **Data Issues: Underreporting** of events by patients and healthcare professionals, and the issue of **incomplete or poor-quality data** in the reports received.
- **Workload:** High case volume due to global drug use and digital submissions, alongside difficulties in prioritizing serious events.
- **Regulatory Complexity:** Pressure from **strict and varying reporting timelines** and constant updates in global regulations

14. CONCLUSION

The research article concludes that **Adverse Event (AE) and case processing is indispensable to modern pharmacovigilance**, serving as the operational and analytical foundation for drug safety.

The continuous, structured collection, validation, and assessment of AE reports allow regulatory authorities and pharmaceutical companies to **meet their ethical, legal, and regulatory obligations** [9]. Crucially, the process successfully translates raw patient reports into **structured data** (the ICSR) that is essential for:

1. **Early and proactive detection** of new or rare safety issues.
2. **Maintaining the therapeutic benefit-risk balance** of all medicinal products.

While the process is challenged by high volumes, data quality issues, and resource limitations, the ongoing adoption of **Pharmacovigilance database** is viewed as the necessary path forward to increase the speed and quality of case processing, thereby strengthening global drug safety systems

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