DEPTH OF BIOLOGY

Unit - 5

Methods,ADR reporting and tools used in Pharmacovigilance
International classification of diseases,
International Non-
proprietary names for drugs, Passive and Active surveillance, Comparative observational studies, Targeted clinical investigations and Vaccine safety surveillance. Spontaneous reporting system and Reporting to regulatory authorities, Guidelines for ADRs reporting. Argus, Aris G Pharmacovigilance, VigiFlow, Statistical methods for evaluating medication safety data.

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Methods, ADR Reporting, and Tools Used in Pharmacovigilance

Pharmacovigilance (PV): Science of detecting, assessing, and preventing adverse drug reactions (ADRs).

ADR reporting is the backbone of PV.

Proper methods and tools help in early detection, evaluation, and prevention of ADRs.

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Methods of ADR Reporting-

A. Spontaneous Reporting-

Most common method.

Healthcare professionals or patients report ADRs voluntarily.

Example: Yellow Card Scheme (UK), PvPI ADR reporting form (India).

Advantages: Easy, simple, cost-effective.

Limitations: Under-reporting, may miss rare ADRs.

B. Case Reports and Case Series-

Detailed description of one or more patients experiencing ADR.

Used for early identification of new ADRs.

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C. Cohort Event Monitoring (CEM)-

Follows a group of patients prescribed a drug over time.
Monitors all events and detects drug-related risks.

D. Targeted Spontaneous Reporting-

Focuses on specific ADRs or high-risk drugs.
Reduces unnecessary reporting and improves data quality.

E. Electronic Health Record (EHR) Mining-
Uses hospital records and databases to detect ADR signals automatically.

F. Registries and Observational Studies-
Large databases of patients on certain drugs.
Helps detect rare or long-term ADRs.

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ADR Reporting in Practice-

Steps in ADR Reporting:

- Detection: Identify an adverse drug reaction in patient care.
- Documentation: Fill ADR reporting form (WHO, PvPI, FDA forms).

-Assessment:

Causality assessment (WHO-UMC, Naranjo scale)

Severity and seriousness assessment

-Submission: Send report to:

Hospital PV centre (AMC)

National PV centre (PvPI, CDSCO)

-Follow-up: Additional info if needed.

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Tools Used in Pharmacovigilance-

A. ADR Reporting Forms-

Standardized forms used to report ADRs.

Examples:

WHO ADR Reporting Form

PvPI ADR Form (India)

FDA MedWatch Form (US)

B. Mobile Applications-

Example: PvPI mobile app for direct reporting by healthcare professionals.

C. Databases and Software-

VigiBase (WHO-UMC): Global ADR database.

EudraVigilance (EMA): ADR database for Europe.

FAERS (FDA): ADR database for the USA.

Signal detection software: Tools to detect safety signals automatically.

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D. Risk Management Tools-

Causality assessment scales: WHO-UMC, Naranjo.

Severity & seriousness scales: Hartwig's scale, CTCAE.

Preventability tools: Schumock and Thornton criteria.

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International Classification of Diseases (ICD)

Introduction-

The International Classification of Diseases (ICD) is a global standard system for classifying diseases and health conditions.

Developed and maintained by the World Health Organization (WHO).

Provides a common language for doctors, researchers, and policymakers.

ICD is not only for diseases, but also for-

Symptoms
Injuries
Causes of death
External factors affecting health

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Objectives of ICD (International Classification of Diseases)-

Standardization – To provide a uniform system for classifying diseases worldwide.

Communication – To create a common medical language for doctors and researchers.

Epidemiology – To study patterns, causes, and frequency of diseases.

Research – To support clinical research and drug safety studies.

Healthcare Planning – To help governments plan health services and resources.

Policy Making – To guide national and international health programmes.

Legal and Insurance Use – To support medical billing, insurance claims, and legal records.

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History and Evolution of ICD-

1893: First international classification prepared by Jacques Bertillon (French statistician).

1948: WHO took responsibility; ICD-6 released (first version under WHO).

1965–1977: ICD-8 and ICD-9 widely used.

1990: ICD-10 adopted by WHO (implemented in 1994, widely used for 20+ years).

2018: ICD-11 approved by World Health Assembly.

2022: ICD-11 officially came into effect for member countries.

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Structure of ICD-

ICD-10
Alphanumeric coding system: one letter + 2–4 numbers.
Codes range from A00–Z99.

Example codes:
A00 → Cholera
I10 → Essential hypertension
E11 → Type 2 diabetes mellitus
J45 → Asthma

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Uses of ICD-

A. In Clinical Practice-

Coding patient diagnoses in hospital records.
Helps in maintaining uniform medical charts.
Facilitates referral and continuity of care.

B. In Research and Public Health-

Used in epidemiological studies (study of disease distribution).
Helps detect and monitor disease outbreaks (e.g., COVID-19 assigned ICD-10 code U07.1).
Guides drug safety studies and pharmacovigilance.

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C. In Health Policy and Administration-

Helps governments plan health budgets.

Identifies priority diseases needing attention.

Guides national health programmes (like TB, diabetes, cancer).

D. In Insurance and Legal Systems-

Provides codes for billing and reimbursement.

Reduces disputes by having standard classifications.

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6. Advantages of ICD-

Provides global uniformity in health statistics.
Helps in comparisons across time and countries.
Useful for drug safety monitoring.
Strengthens data-driven health policies.

7. Limitations of ICD-

Requires regular updating to include new diseases.
Adoption of ICD-11 may be slow in low-resource countries.
Some cultural/clinical variations may not be perfectly covered.

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International Non-Proprietary Names (INN) for Drugs

Every drug has many names → chemical name, brand name, and generic name.
To avoid confusion, the World Health Organization (WHO) introduced the system of International Non-Proprietary Names (INN).

An INN is the official generic name of a drug, recognized worldwide.

Example-
Chemical name: N-acetyl-para-aminophenol
INN (generic): Paracetamol
Brand names: Crocin, Calpol, Dolo-650, etc.

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Objectives of INN System-

Unique Identification – Each drug has a single, unique generic name worldwide.

Avoid Confusion – Prevents mistakes due to multiple brand names.

Communication – Provides a common language for doctors, pharmacists, and scientists globally.

Public Health Safety – Reduces medication errors.

Universal Acceptance – Makes drug names easy to use in different countries and languages.

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3. Characteristics of INN-

Simple and short (easy to pronounce).
Universally accepted across countries.
Clear and non-confusing (not too similar to other drug names).
Free from commercial influence (not linked to any company).
Often use common "stems" to indicate drug class.

Examples of stems:

-pril → ACE inhibitors (Enalapril, Lisinopril)
-olol → Beta blockers (Propranolol, Atenolol)
-mab → Monoclonal antibodies (Trastuzumab, Adalimumab)
-statin → Lipid-lowering drugs (Atorvastatin, Simvastatin)

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4. Process of Naming (How INN is given?)

Pharmaceutical company applies to WHO for a new drug name.

WHO reviews the application and suggests a name.

Name is checked for:

Uniqueness

No similarity with existing names

Easy pronunciation in different languages

After approval → drug gets an official INN.

5. Importance of INN

Ensures safe prescribing and dispensing.

Facilitates education and training of healthcare professionals.

Used in pharmacovigilance (monitoring drug safety).

Promotes fair competition (not linked to brand marketing).

Essential for international trade and regulation of medicines.

Passive and Active Surveillance in Pharmacovigilance

Introduction-

Surveillance in pharmacovigilance = continuous monitoring of drugs for Adverse Drug Reactions (ADRs) after they are marketed.

Two main methods:

Passive surveillance

Active surveillance

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1. Active Surveillance-

Definition-

Active surveillance is a method where systematic efforts are made to detect and record ADRs by actively monitoring patients.

Instead of waiting for voluntary reports, data is actively collected by investigators, hospitals, or registries.

Key Features-

Requires organized programmes and follow-ups.

Collects complete and reliable information.

Uses structured methods like cohort studies, patient monitoring, and registries.

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Methods of Active Surveillance-

1. Cohort Event Monitoring (CEM):
A group (cohort) of patients on a new medicine is followed regularly.
ADRs are recorded systematically.
Example: Monitoring new HIV or TB medicines.

2. Prescription Event Monitoring (PEM):
Prescriptions of a drug are monitored to track outcomes.
Physicians report events after prescribing.

3. Registries:
Databases for specific diseases or drugs (e.g., vaccine registries, cancer drug registries).

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Advantages-

Provides detailed and reliable data.
Can calculate incidence and risk of ADRs.
Detects both known and unknown ADRs.
Reduces reporting bias compared to passive methods.

Limitations-

Expensive and time-consuming.
Requires trained staff and infrastructure.
May not cover very large populations due to cost.

Examples

COVID-19 vaccine monitoring programmes (active follow-up of vaccinated people).

Cancer drug registries tracking long-term ADRs.

WHO's Cohort Event Monitoring in African countries for anti-malarials.

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2. Passive Surveillance-

Definition

Passive surveillance is a method where reports of adverse drug reactions (ADRs) are received voluntarily from healthcare professionals, patients, or pharmaceutical companies.
It is also called the Spontaneous Reporting System (SRS).

Key Features

Relies on voluntary submission of reports.
Data is usually collected through:
ADR reporting forms (paper or online)
Yellow card system (UK), MedWatch (USA), VigiFlow (WHO)
Involves large populations without active follow-up.

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Advantages

Simple and inexpensive → easy to implement.
Covers entire population → any healthcare worker/patient can report.
Effective for detecting rare ADRs (not seen in clinical trials).
Provides early warnings about new safety signals.

Limitations

Under-reporting → many ADRs are never reported.
Reporting bias → only severe or unusual reactions may be reported.
Incomplete data → reports may lack dose, timing, or patient history.
Cannot provide exact incidence or prevalence of ADRs.

Examples

UK's Yellow Card Scheme for ADR reporting.
India's PvPI ADR reporting forms collected at Pharmacovigilance Centres.
US FDA MedWatch programme.

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Comparative Observational Studies

Observational studies are research designs where the investigator does not intervene or assign treatments; instead, they observe and analyze events as they naturally occur.

In comparative observational studies, researchers compare two or more groups (such as exposed vs. unexposed, diseased vs. non-diseased) to identify differences in outcomes.

Unlike experimental studies (like RCTs), there is no randomization.

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Purpose-

To study the association between exposure (e.g., drug, lifestyle, risk factor) and outcomes (e.g., disease occurrence, recovery).

Useful when experimental studies are unethical or impractical (e.g., cannot expose people to smoking just to study lung cancer).

Helps generate real-world evidence.

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Types of Comparative Observational Studies-

1. Cohort Studies-

Groups are defined based on exposure status (exposed vs. unexposed).
Followed over time to compare incidence of disease/outcome.

Example: Following smokers and non-smokers to see who develops lung cancer.

2. Case–Control Studies
Groups are defined based on disease status (cases = diseased, controls = non-diseased).

Past exposures are compared between groups.
Example: Comparing past smoking history in lung cancer patients vs. healthy individuals.

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3. Cross-Sectional Studies (Comparative Type)-

Data collected at one point in time.
Compares prevalence of disease/exposure between groups.

Example: Comparing prevalence of hypertension among urban vs. rural populations.

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Advantages-

Practical and less expensive than RCTs.

Ethical (no forced interventions).

Can study rare exposures (cohort) or rare diseases (case-control).

Provide real-world evidence.

Limitations-

Cannot prove causality (only association).

Subject to bias:

Selection bias (improper group selection)

Recall bias (inaccurate memory of exposure in case-control)

Confounding factors (e.g., lifestyle, genetics).

Less control over external factors compared to experimental studies.

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Targeted Clinical Investigations

Drug safety is a very important part of pharmacovigilance. After a medicine is approved and marketed, new safety concerns may appear in the population that were not detected during pre-marketing clinical trials.

In such cases, normal spontaneous reporting may not be enough to clarify the risk. For this reason, targeted clinical investigations (TCIs) are performed.

Definition

Targeted clinical investigations are planned and focused studies that are carried out to investigate a specific safety concern, adverse event, or suspected risk associated with a particular drug or vaccine.

They are usually conducted after the drug is available in the market (post-marketing phase).

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Objectives of Targeted Clinical Investigations -

To verify whether a suspected adverse drug reaction is truly caused by the medicine.

To understand the frequency, severity, and risk factors of the adverse event.

To study safety in special populations such as pregnant women, elderly, children, or patients with kidney/liver problems.

To provide scientific evidence for regulatory decision-making (label changes, warnings, or withdrawal).

To improve the benefit–risk profile of the medicine.

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Characteristics-

They are problem-oriented and focus only on one particular safety issue.

Can be observational (case–control, cohort) or interventional (special clinical trial).

Carried out in hospitals, clinics, or through registries.

Require protocols, ethics approval, and informed consent when interventional.

Examples

A targeted study on cardiovascular risk of COX-2 inhibitors (rofecoxib).

Investigation of hepatotoxicity in patients treated with anti-tuberculosis drugs.

Study on psychiatric side effects of isotretinoin in young patients.

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Advantages-

Provides stronger evidence than routine ADR reports.

Focused on the exact problem rather than general monitoring.

Helps in identifying at-risk groups.

Improves public safety and guides rational drug use.

Limitations-

Expensive and time consuming.

Cannot study other unrelated ADRs.

May require large sample sizes for rare events.

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Vaccine Safety Surveillance

Introduction-

Vaccines are given to healthy individuals, including children, so their safety standards must be extremely high.

Although vaccines undergo rigorous testing before approval, rare or long-term adverse events may only be detected after widespread use in the population.

For this reason, every country establishes vaccine safety surveillance systems to continuously monitor and evaluate adverse events following immunization (AEFI).

Definition-

Vaccine safety surveillance is a continuous and systematic process of collecting, analyzing, and assessing adverse events after immunization, with the aim of ensuring that vaccines remain safe, effective, and trusted in the community.

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Objectives-

To detect previously unknown or rare adverse events.

To monitor the frequency and severity of known adverse reactions.

To identify risk factors for vaccine-related adverse events.

To provide information for public health policies.

To maintain public confidence in immunization programs.

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Types of Surveillance-

1. Passive Surveillance
Relies on voluntary reporting of AEFI by healthcare workers or patients.

2. Active Surveillance-

Systematic effort to actively look for cases of AEFI.

Involves follow-up of vaccinated individuals through hospital monitoring or electronic health records.

3. Targeted Studies-

Case–control or cohort studies done when a specific vaccine–adverse event link is suspected.
Example: Studying risk of blood clots after COVID-19 vaccines.

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Examples of Vaccine Safety Surveillance-

Surveillance of allergic reactions after COVID-19 vaccines.

Monitoring for Guillain-Barré Syndrome (GBS) after influenza vaccination.

Safety checks for HPV vaccines in adolescents.

Polio vaccine surveillance for vaccine-associated paralytic polio.

Advantages

Builds and maintains public trust in immunization.

Detects rare or unexpected adverse events early.

Provides evidence for modifying vaccine policies.

Ensures long-term safety of immunization programs.

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Spontaneous reporting system and Reporting to regulatory authorities

Spontaneous reporting is the backbone of pharmacovigilance worldwide.

It is the simplest and most widely used method for detecting adverse drug reactions (ADRs) once a medicine is marketed.

In this system, reports of suspected ADRs are collected from healthcare professionals, patients, and pharmaceutical companies without any active attempt to seek them out.

It helps in early detection of new, rare, or serious adverse reactions and is essential for maintaining the benefit-risk balance of medicines.

A spontaneous reporting system (SRS) is a pharmacovigilance method where healthcare professionals, patients, or manufacturers voluntarily report suspected adverse drug reactions to a central pharmacovigilance center or authority.

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Objectives-

To identify new or unexpected ADRs not detected during clinical trials.

To monitor the frequency and seriousness of known ADRs.

To detect drug interactions, medication errors, and product quality defects.

To provide data for regulatory decisions such as warnings, restriction of use, or withdrawal.

To create a database of ADRs for signal detection and risk assessment.

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Examples of Spontaneous Reporting Systems-

India: PvPI (Pharmacovigilance Programme of India) under IPC (Indian Pharmacopoeia Commission).

USA: MedWatch – FDA Adverse Event Reporting System (FAERS).

UK: Yellow Card Scheme (MHRA).

WHO: VigiBase, managed by the Uppsala Monitoring Centre (Sweden).

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Advantages-

Simple, inexpensive, and covers entire population.

Effective in detecting rare, serious, and unexpected ADRs.

Provides a global pool of safety data.

Helps in signal detection (early warnings).

Limitations-

Underreporting is the biggest problem (only 5–10% ADRs are reported).

Quality of reports may be poor or incomplete.

Cannot calculate true incidence rates (no denominator data).

Subject to reporting bias (serious ADRs reported more than mild ones).

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Reporting to Regulatory Authorities-

Introduction-

Once ADRs are reported through spontaneous systems or identified in studies, they must be forwarded to regulatory authorities.

Regulatory authorities are national or international bodies responsible for ensuring the safety, efficacy, and quality of medicines.

Reporting ADRs to these bodies ensures that safety signals are properly evaluated and appropriate regulatory action is taken.

Who Reports?

Healthcare Professionals (doctors, nurses, pharmacists, dentists).
Patients and Consumers.
Pharmaceutical Companies (mandatory reporting of ADRs for marketed drugs).
Pharmacovigilance Centres at hospital, regional, or national level.

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What Should Be Reported?

All serious ADRs (life-threatening, requiring hospitalization, causing disability or death).

Unexpected ADRs (not mentioned in product labeling).

Lack of efficacy of medicines (especially vaccines, antimicrobials).

Medication errors, misuse, or abuse.

Quality issues (contamination, counterfeit drugs).

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National Regulatory Authorities-

India: Central Drugs Standard Control Organization (CDSCO), under Ministry of Health and Family Welfare. ADRs are collected through PvPI and forwarded to CDSCO.

USA: Food and Drug Administration (FDA). ADRs submitted via MedWatch are stored in FAERS.

Europe: European Medicines Agency (EMA). Reports collected in EudraVigilance database.

WHO: Global database VigiBase managed by Uppsala Monitoring Centre.

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Process of Reporting

Reporter fills ADR reporting form (paper or online).

Report submitted to local hospital or regional pharmacovigilance center.

Data verified and entered into national pharmacovigilance database.

Signals detected are forwarded to the regulatory authority.

Regulatory authority evaluates the signal and takes appropriate action.

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Advantages of Reporting to Regulatory Authorities-

Ensures national and global monitoring of drug safety.

Promotes standardization of ADR data.

Helps in regulatory decision-making.

Improves public trust in medicines.

Challenges-

Lack of awareness among healthcare professionals.

Fear of legal consequences in some cases.

Incomplete or delayed reports.

Heavy workload for regulators in analyzing thousands of reports.

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Guidelines for ADR Reporting

Adverse drug reactions (ADRs) are unwanted or harmful effects that occur after the administration of a drug at normal doses.

Monitoring ADRs is an essential part of pharmacovigilance, as it ensures the continued safety of medicines after they are marketed.

To achieve this, proper guidelines for ADR reporting have been developed at national and international levels.

These guidelines explain what to report, who should report, when to report, and how to report ADRs.

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Who Should Report ADRs?

According to international and national guidelines, ADRs can be reported by:

Healthcare professionals – doctors, nurses, dentists, pharmacists, AYUSH practitioners.

Pharmaceutical companies – mandatory reporting of ADRs related to their products.

Patients and consumers – through patient reporting forms or online portals.

Clinical trial investigators – reporting ADRs during clinical research.

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What ADRs Should Be Reported?

Guidelines emphasize that the following must be reported:

-Serious ADRs
Life-threatening events.
Requiring hospitalization or prolonging hospital stay.
Causing significant disability or death.

-Unexpected ADRs
Not mentioned in the product labeling or package insert.

-All suspected ADRs for new drugs
For drugs introduced recently in the market (first 2-3 years).

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-Special cases

ADRs in children, pregnant women, elderly.

Lack of efficacy (especially in vaccines or antimicrobial drugs).

Suspected counterfeit or substandard products.

Medication errors, misuse, or drug abuse.

When to Report ADRs?

As soon as possible after detection.
Serious and unexpected ADRs should be reported within 24 hours.
For pharmaceutical companies:
Serious ADRs – report to regulatory authorities within 15 calendar days.
Non-serious ADRs – usually reported in periodic safety update reports (PSURs).

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How to Report ADRs?

ADR reporting can be done using standard formats provided by national or international pharmacovigilance authorities.

Steps in ADR Reporting-

1. Collect information -

Patient details (age, sex, medical history).

Suspected drug (name, dose, route, duration).

Description of adverse event.

Concomitant medications.

Outcome of the reaction.

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Fill the ADR reporting form:

India: Suspected ADR Reporting Form by PvPI.
WHO: Individual Case Safety Report (ICSR).
USA: MedWatch FDA Form 3500.
UK: Yellow Card Form.

Submit the form:

Hospital Pharmacovigilance Committee.
Regional Pharmacovigilance Centres.
Directly to national regulatory authority (e.g., CDSCO in India, FDA in USA, EMA in Europe).
Online portals or mobile applications are also available.

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- International Guidelines-

Several international organizations have established clear ADR reporting guidelines:

WHO (World Health Organization)-

Operates the Programme for International Drug Monitoring.

Uses the global database VigiBase at the Uppsala Monitoring Centre (Sweden).

Provides ICSR format for standardized ADR reporting.

ICH (International Council for Harmonisation)-

Provides guidelines on expedited reporting of serious and unexpected ADRs (E2A guideline).

Requires companies to report serious ADRs within 15 days.

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-US FDA (Food and Drug Administration)

ADRs reported via MedWatch system.
Companies must submit Individual Case Safety Reports (ICSRs).

-EMA (European Medicines Agency)

Uses EudraVigilance database.
Follows Good Pharmacovigilance Practices (GVP) Module VI for ADR reporting.

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National Guidelines (India Example)-

-Pharmacovigilance Programme of India (PvPI), coordinated by Indian Pharmacopoeia Commission.

-ADRs can be reported by healthcare workers, patients, or industry.

-Reports are collected through:

ADR reporting forms (paper/online).
PvPI mobile app.
Toll-free helpline number.

-Reports are forwarded to CDSCO (Central Drugs Standard Control Organization).

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Importance of Following Guidelines-

Ensures uniformity and quality of data.

Helps in timely signal detection.

Facilitates global collaboration and data sharing.

Protects patients from unsafe medicines.

Increases awareness and responsibility among healthcare providers.

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Argus, Aris G Pharmacovigilance, VigiFlow

Pharmacovigilance is the science of monitoring, detecting, assessing, and preventing adverse drug reactions (ADRs) and other drug-related problems.

With the increasing number of medicines and the large volume of safety data generated worldwide, manual pharmacovigilance systems are not sufficient.

To manage this huge data, specialized pharmacovigilance software systems have been developed.

These systems help in the collection, storage, analysis, and reporting of Individual Case Safety Reports (ICSRs) to national and international regulatory authorities. Among the most widely used systems are Oracle Argus Safety, ArisG, and VigiFlow.

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1. Argus Safety-

Introduction-

Oracle Argus Safety is one of the most widely used drug safety management systems.

It is used by pharmaceutical companies, contract research organizations (CROs), and regulatory authorities to manage pharmacovigilance activities.

It supports compliance with international guidelines such as ICH, FDA, EMA, and WHO requirements.

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Functions-

Case Management – Entry, tracking, and processing of ICSRs.

Signal Detection – Identifying trends and new safety signals.

Regulatory Reporting – Automatic generation and submission of reports to authorities (e.g., FDA, EMA, CDSCO).

Workflow Management – Ensures timely case processing within reporting timelines.

Integration – Can connect with other databases like clinical trial management systems.

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Features-

Cloud-based and scalable.

User-friendly dashboards.

Global compliance (supports E2B, MedDRA, WHO-Drug).

Supports risk management and periodic safety update reports (PSURs/PBRERs).

Advantages-

Widely accepted by multinational pharmaceutical companies.

Reduces manual workload.

Helps in meeting strict regulatory deadlines.

Limitations-

Expensive to implement.

Requires technical expertise and training.

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ArisG Pharmacovigilance-

Introduction

ArisG is another leading pharmacovigilance software, developed by ArisGlobal.

It is used for the collection, coding, assessment, and reporting of adverse events.

Like Argus, it complies with international pharmacovigilance standards (ICH E2B, MedDRA coding).

Functions-

Case Processing – Handling spontaneous reports, literature cases, clinical trial safety data.

Regulatory Submissions – Direct electronic submissions to FDA (FAERS), EMA (EudraVigilance), and other agencies.

Data Mining and Signal Detection – Detects patterns of ADRs.

Automation – Automatic case intake from emails, safety databases, and portals.
Workflow Tracking – Monitors the case status from receipt to closure.

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Features-

Cloud-based and integrated with other ArisGlobal modules.

Uses MedDRA and WHO-Drug dictionaries for standard coding.

Facilitates global safety reporting.

Advantages-

Reduces duplication and errors.

Strong automation features.

Provides end-to-end pharmacovigilance solution.

Limitations-

Costly for smaller organizations.

Requires trained users.

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3. VigiFlow-

Introduction

VigiFlow is a web-based pharmacovigilance management system developed by the Uppsala Monitoring Centre (UMC), Sweden, under the WHO Programme for International Drug Monitoring.

It is mainly used by national pharmacovigilance centres in low- and middle-income countries.

It provides an easy and affordable way for countries to participate in global pharmacovigilance.

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Functions-

Case Reporting – Collects, stores, and manages Individual Case Safety Reports (ICSRs).

Data Sharing – Transfers reports to the global WHO database VigiBase.

Coding – Uses MedDRA and WHO Drug dictionaries for coding of events and medicines.

Security – Ensures data confidentiality and secure transmission.

Multilingual Support – Available in different languages for global use.

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Features

Simple online platform (no need for complex installations).

Can be accessed from anywhere with internet.

Supports both national and regional pharmacovigilance centres.

Provides automatic generation of reports in ICH E2B format.

Advantages

Affordable and practical for developing countries.

Maintained and updated by WHO-UMC.

Ensures global data standardization.

Directly linked with VigiBase, the largest international ADR database.

Limitations

Limited customization compared to Argus or ArisG.

Mainly designed for national authorities, not large pharma companies.

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Statistical Methods for Evaluating Medication Safety Data

Introduction-

The safety of medicines is a crucial part of pharmacovigilance. Once a drug is marketed and used by a large population, huge amounts of safety data are generated from spontaneous reports, clinical trials, observational studies, and electronic health records.

To analyze this data and detect potential risks, statistical methods are widely used. These methods help in:

-Identifying new or unexpected adverse drug reactions (ADRs).
-Estimating the frequency and strength of associations.
-Differentiating true safety signals from random variations.
-Supporting regulatory decision-making.

Thus, statistical tools are essential for evaluating medication safety data in both national and international pharmacovigilance systems.

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After medicines are approved, they are used by millions of people.

Some side effects (ADRs) are rare and may not appear in clinical trials.

To check medicine safety, we use statistics (numbers, calculations, comparisons).

These methods help us find, measure, and confirm if a drug is really linked to an adverse event.

1. Simple Statistics (Descriptive Statistics)-

First step: just count and describe the data.
Example:

100 people reported headache after Drug A.
60% were female, 40% male.
Average age = 45 years.
This gives a basic idea of the safety problem.

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Disproportionality Analysis (Finding "Signals")-

This is the most common method in pharmacovigilance.
It checks if a drug–ADR pair is reported more often than expected.

-Proportional Reporting Ratio (PRR):
Compares % of an ADR with one drug vs. all other drugs.
Example: If 20% of reports for Drug A are rashes, but only 5% for all drugs → possible signal.

-Reporting Odds Ratio (ROR):
Compares the odds of getting ADR with the drug vs. other drugs.

-Chi-square Test:
A math test to check if the difference is real, not by chance.

-Bayesian methods (BCPNN, EBGM):
Advanced methods used by WHO and FDA.
Reduce false alarms, especially when data is small.

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#Observational Study Statistics-

Sometimes, researchers do special studies (cohort or case–control).
-Relative Risk (RR):
Risk of ADR in drug users ÷ risk in non-users.
-Odds Ratio (OR):
Odds of ADR in cases ÷ odds in controls.
-Hazard Ratio (HR):
Measures ADR over time (time-to-event).

Example: If RR = 3, it means drug users have 3 times higher risk of that ADR.

#Advanced Methods-

Regression Models: Adjust results for age, gender, other diseases.

Meta-analysis: Combines many studies together → more accurate.

Machine learning/Data mining: Computers find patterns in huge data.

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Vaccine Safety Statistics-

For vaccines, special methods are used:
-Observed vs. Expected Analysis:
Compare how many ADRs happened after vaccination vs. how many normally happen in the population.
-Self-Controlled Case Series (SCCS):
The same person is compared during "risk period" vs. "safe period."
-Case-crossover studies:
Compares exposure during ADR time vs. other times in the same person.

Challenges

Not all ADRs are reported → underreporting.
Some events may happen by coincidence, not drug.
Results may be confusing if patients take many drugs.
Statistics only show association, doctors must decide if it's causation.

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