BP705T · B.Pharm Semester VII · Theory Notes

Pharmacovigilance

Unit III — Adverse Drug Reactions

Unit III (8 hours)

Pills & Python Notes

From-zero teaching standard: every technical term is defined before use.

Syllabus coverage: Unit III (8 hours).

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CHAPTER 8: Adverse Drug Reactions — Classification, Types, Mechanisms and Risk Factors

Learning Objectives

After studying this chapter, the student should be able to:

1 Define an adverse drug reaction (ADR) and an adverse drug event (ADE) in simple words.

2 Classify ADRs into types A, B, C, D, E and F with examples.

3 Explain Type A and Type B reactions and the differences between them.

4 Describe the main mechanisms that cause ADRs — dose-related (pharmacological), allergic (immunological), idiosyncratic (genetic), and interaction-based.

5 List patient-related, drug-related, and disease-related risk factors for ADRs.

6 Explain why children, elderly people, pregnant women and kidney/liver patients face higher ADR risk.

7 Classify ADRs by organ system and by onset/severity when relevant.

Definitions

Adverse Drug Reaction (ADR). An adverse drug reaction is any harmful and unwanted effect of a medicine that happens when the medicine is used at a normal, approved dose for prevention, diagnosis or treatment of a disease. Key points in this definition: (a) the effect is harmful, (b) it is unwanted — the patient did not take the drug for this effect, and (c) it happens at a normal dose, not because of an overdose or a mistake. This is the classic WHO definition of ADR.

Adverse Drug Event (ADE). An adverse drug event is any bad health event that happens while a patient is taking a medicine, but we are not sure whether the medicine caused it. So every ADR is an ADE, but not every ADE is an ADR. Example: a patient taking a blood pressure tablet has a headache. The headache is an ADE. If we later confirm the tablet caused the headache, it becomes an ADR.

Side effect. A side effect is an expected, usually mild and known effect of a drug that is not the main therapeutic purpose but is an accepted consequence at normal doses. Example: drowsiness with an antihistamine.

Toxic effect. A toxic effect is harm caused when the drug level in the body is too high — due to overdose, wrong dose, or the body not removing the drug properly.

Drug allergy. A drug allergy is a harmful response caused by the body's immune system (defence system) reacting wrongly to a drug. It is not related to the dose.

Idiosyncratic reaction. An idiosyncratic reaction is a strange, unpredictable reaction that happens in only a few people, often because of their unique body chemistry or genes.

Terminology table

Term	Simple meaning
ADR (Adverse Drug Reaction)	Harmful, unwanted effect of a medicine at a normal dose
ADE (Adverse Drug Event)	Any bad event during drug use; cause may or may not be the drug
Side effect	Expected, usually mild unwanted effect at normal dose
Toxic effect	Harm from too much drug in the body (overdose or poor elimination)
Drug allergy	Immune system wrongly attacks the drug as if it were a germ
Idiosyncrasy	Rare, strange reaction linked to a person's unique body chemistry/genes
Teratogenicity	A drug causing birth defects in the unborn baby
Carcinogenicity	A drug or chemical increasing the risk of cancer
Onset	The time when the reaction first appears after starting the drug
Dose-related	The reaction becomes stronger as the dose increases
Immunological	Related to the body's immune (defence) system
Ototoxicity	Drug damage to the ears/hearing
Nephrotoxicity	Drug damage to the kidneys
Hepatotoxicity	Drug damage to the liver
Hemolysis	Breaking open of red blood cells

Simple explanations

What is an ADR in one line? No medicine is perfect. A medicine is given to cure a disease, but in some patients it also causes harm that was not wanted. That unwanted harm at a normal dose is an adverse drug reaction. Think of a medicine as a key that is supposed to open one lock (cure the disease). Sometimes the same key accidentally opens other locks in the body (other organs), and that causes trouble — those troubles are ADRs.

Why do ADRs happen at normal doses? Because every human body is slightly different. The "normal dose" is calculated from studies on thousands of people, but one individual may absorb, process, or react to the drug differently. Also, many drugs act on targets that exist in more than one organ — the drug cannot be told to "go only to the sick organ."

Why do we study ADRs? ADRs are a major cause of hospital admissions, and most can be prevented or managed if health workers know what to look for. Pharmacists are the last checkpoint before a medicine reaches the patient.

Classifications

1. Classification of ADRs into types (Rawlins and Thompson classification — extended A to F)

This is the most famous and most exam-important classification of ADRs.

Type	Name	Meaning in simple words	Common or rare	Example
Type A	Augmented	An exaggerated, stronger version of the drug's normal action — dose-related and predictable	Common (~80% of ADRs)	Bleeding from the blood-thinner warfarin; low blood sugar from too-strong insulin action
Type B	Bizarre	Strange, unexpected reactions not related to the drug's normal action — not dose-related	Uncommon	Allergy to penicillin; malignant hyperthermia with general anaesthetics
Type C	Chronic	Reactions that appear after long-term (chronic) use	Depends on duration	Steroid-induced cataract or diabetes after months of corticosteroids
Type D	Delayed	Reactions that appear a long time after the drug is stopped	Rare	Cancer after many years of certain immunosuppressants; birth defects
Type E	End of use	Reactions that appear when a drug is suddenly withdrawn	Predictable on stopping	Rebound high blood pressure after stopping clonidine suddenly
Type F	Failure of therapy	The drug fails to work — a common reason is a drug interaction or wrong dose	Common	Contraceptive failure when antibiotics reduce its effect; antibiotic resistance

Key takeaway: Types A and B are the "classic two" asked most in exams.

2. Classification by predictability

- **Predictable ADRs:** We can expect them from the drug's known action (Type A). Example: constipation with codeine.
- **Unpredictable ADRs:** They surprise us (Type B). Example: anaphylaxis to penicillin in a person who never reacted before.

3. Classification by organ system affected

System	Examples
Skin	Rash, itching, hives, Stevens–Johnson syndrome
Gut (GI)	Nausea, vomiting, diarrhoea, constipation, stomach ulcer
Liver	Hepatitis, jaundice (drug-induced liver injury)
Kidney	Kidney failure from aminoglycosides or NSAIDs
Blood	Anaemia, low white cells, bleeding
Heart	Irregular heartbeat, low blood pressure
Nervous system	Dizziness, drowsiness, seizures
Ear	Hearing loss (ototoxicity)

Mechanisms and processes

Mechanism means "how does the reaction happen inside the body." The main mechanisms are:

Mechanism 1: Pharmacological (dose-related) mechanism

Technical concept: The drug acts on its target receptor or enzyme more strongly than needed, or acts on the same type of target in other organs.

Simple explanation: The drug is doing its normal job, but doing it too much. Like pressing the accelerator of a car too hard.

Example: Warfarin thins the blood to prevent clots. If the dose is too high, blood becomes too thin and the patient bleeds. The mechanism (stopping clotting) is the drug's normal action — just exaggerated.

Mechanism 2: Immunological (allergic) mechanism

Technical concept: The immune system mistakes the drug (or a drug-protein complex) for an invader and attacks it, releasing chemicals like histamine.

Simple explanation: The body's defence soldiers mistake a friendly visitor (the medicine) for an enemy and start a war inside the body.

Example: Penicillin allergy — the immune system produces antibodies against penicillin, causing rash, swelling or, in severe cases, anaphylaxis (sudden dangerous fall in blood pressure with breathing difficulty).

Mechanism 3: Idiosyncratic (genetic) mechanism

Technical concept: Some people carry genes that make special enzymes missing or abnormal, so the drug is converted into a harmful product, or the body reacts in an unusual way.

Simple explanation: It is written in the person's genes — like a rare family trait. The drug is safe for 999 people but harms 1 person because of their unique body chemistry.

Example: Primaquine (an antimalarial) causes destruction of red blood cells (hemolysis) in people with G6PD enzyme deficiency — a genetic condition common in some populations.

Mechanism 4: Drug interaction mechanism

Technical concept: One drug changes how another drug is absorbed, distributed, broken down or removed, raising its level to toxic range or blocking its effect.

Simple explanation: Two medicines meet inside the body and fight or help each other, changing each other's strength.

Example: The antibiotic erythromycin blocks the liver enzyme that removes the heart drug digoxin, so digoxin builds up to toxic levels.

Mechanism 5: Product-quality-related mechanism

Simple explanation: Sometimes the problem is not the drug molecule but the product — contamination or a wrong dose in the tablet. These are quality problems rather than true ADRs, but they reach the patient the same way.

Flowchart: How an ADR develops (general pathway)

```
Patient takes medicine at normal dose
        |
        v
Drug enters blood → reaches body tissues
        |
        v
Drug meets its target (receptor/enzyme) — WANTED action
        |
        v
Drug ALSO meets targets in other organs / wrong people react differently
        |
   +----+----+--------------------------+
   |         |                          |
   v         v                          v
Dose too   Immune system              Genes make a
strong     attacks the drug           strange reaction
(Type A)   (Type B allergic)          (Type B idiosyncratic)
        |
        v
Unwanted harmful effect = ADR
        |
        v
Detect → Assess → Report → Manage
(covered in Chapter 9)
```

Flowchart: Type A vs Type B — how to tell them apart

```
An unwanted effect is noticed
        |
        v
Is it an exaggeration of the drug's KNOWN action?
        |
   YES / \ NO
      /   \
     v     v
  TYPE A  TYPE B
  (Augmented)  (Bizarre)
  - Dose-related      - Not dose-related
  - Predictable       - Unpredictable
  - Common (~80%)     - Uncommon
  - Usually mild–     - Often severe
    moderate
  Example: bleeding   Example: penicillin
  with warfarin       anaphylaxis
```

Infographic concept box

INFOGRAPHIC CONCEPT: "The ADR Iceberg and the 6 Types." Top visual: an iceberg — the visible tip above water labelled "Type A — common, predictable, dose-related (what doctors expect)"; below the water, the large hidden mass labelled "Types B–F — rare, strange, delayed, or withdrawal reactions (what surprises us)." A side panel shows six colour-coded cards: A = Augmented (thermometer rising = more dose, more effect), B = Bizarre (lightning bolt = sudden allergy), C = Chronic (calendar = long-term use), D = Delayed (clock = appears years later), E = End of use (hand letting go = stopping the drug), F = Failure (broken shield = drug stops working). Bottom strip: "Risk factors thermometer" — age extremes, pregnancy, kidney/liver disease, polypharmacy, genetics shown as rising risk bars. Key takeaway banner: "Type A you can predict — Type B you must be ready for."

Tables

Table: Type A vs Type B ADRs (comparison)

Feature	Type A (Augmented)	Type B (Bizarre)
Relation to dose	Dose-related — more dose, more effect	Not dose-related
Predictability	Predictable from drug's known action	Unpredictable
Frequency	Common (~80% of all ADRs)	Uncommon
Mechanism	Exaggerated pharmacological action	Immune (allergic) or genetic (idiosyncratic)
Severity	Usually mild to moderate	Often severe
Management	Reduce dose or stop drug	Stop drug immediately; never re-give
Example	Hypoglycaemia with insulin	Anaphylaxis with penicillin

Table: Risk factors for ADRs

Category	Risk factor	Why it increases risk (simple)
Patient — age	Very young (children) and very old (elderly)	Children's organs still developing; elderly have slow liver/kidney function
Patient — pregnancy	Pregnant women	Drug can reach the unborn baby; body chemistry changes
Patient — genes	Genetic differences (e.g., slow vs fast drug breakdown)	Genes decide how fast the liver destroys the drug
Disease	Kidney disease, liver disease	The body cannot remove or break down the drug, so it builds up
Disease	Multiple diseases at once	More diseases → more drugs → more chances of ADRs
Drug	Polypharmacy (taking many drugs)	More drugs → more interactions and side effects
Drug	Narrow therapeutic index drugs (warfarin, digoxin, lithium)	Small gap between helpful dose and harmful dose
Drug	Long duration of treatment	More time for chronic/delayed reactions to appear
Drug	Previous allergy to the same drug	Immune system remembers — reaction is faster and worse next time

Examples

1. **Type A:** A diabetic patient takes a slightly high insulin dose — blood sugar falls too low (sweating, shaking). The drug's normal action, exaggerated.
2. **Type B:** One penicillin tablet causes lip swelling and breathing difficulty within minutes (anaphylaxis). Normal dose; immune system overreacted.
3. **Type C:** Months of steroid tablets cause cataract and high blood sugar — appears only after chronic use.
4. **Type D:** A drug taken years ago raises cancer risk much later — hardest to link to the drug.

5 **Type E:** Stopping clonidine suddenly shoots blood pressure up dangerously (rebound hypertension).

6 **Type F:** An antibiotic speeds up liver breakdown of birth-control hormones — the contraceptive fails.

7 **Risk factors combined:** An 80-year-old with weak kidneys gets a normal adult antibiotic dose; the drug builds up and damages hearing — age + kidney disease + drug together.

Analogies

1 **Type A — the loudspeaker:** The drug plays the correct song, but the volume is too high. The song (drug action) is right; the volume (dose effect) hurts.

2 **Type B — the bee sting:** Most people get mild pain from a bee sting, but one person in a thousand gets a life-threatening whole-body reaction. Same sting, different immune system.

3 **Risk factors — a weak bridge:** Age, kidney disease and many medicines are extra trucks on a bridge. Each alone is fine, but together the bridge (the patient's body) may crack — that crack is the ADR.

Pharmacy relevance

- The pharmacist is the final safety checkpoint before the medicine reaches the patient. Checking the prescription for wrong doses, dangerous combinations and known patient allergies directly prevents Type A and Type B ADRs.
- Counselling patients about expected side effects (Type A) helps them recognise and report ADRs early instead of silently stopping treatment.
- Pharmacists in ADR Monitoring Centres (AMCs) collect and verify ADR reports — this chapter's classification knowledge is used daily to describe and categorise each reported reaction.
- When dispensing high-risk drugs (warfarin, insulin, digoxin, lithium), the pharmacist must double-check doses and interactions — these narrow-therapeutic-index drugs cause the most serious Type A reactions.
- Knowledge of risk factors guides the pharmacist to give extra counselling to elderly patients, pregnant women and kidney/liver patients.

India context

- India's large population uses many medicines, including fixed-dose combinations and over-the-counter drugs bought without prescriptions — self-medication raises ADR risk, especially from NSAIDs, antibiotics and steroids.
- G6PD deficiency, linked to idiosyncratic reactions like primaquine-induced hemolysis, is found in several Indian communities.
- The Pharmacovigilance Programme of India (PvPI), coordinated by the Indian Pharmacopoeia Commission (IPC), Ghaziabad, collects ADR reports from ADR Monitoring Centres across the country — as per the latest guidelines/notifications, confirm the current edition for reporting procedures.
- Commonly reported ADRs in Indian settings include skin rashes from antibiotics and antiepileptics, and liver injury from anti-tubercular drugs — a major local concern given India's TB burden.

Key points

1 An ADR is a harmful, unwanted effect of a drug at a normal dose.

2 ADE is a broader term — a bad event during drug use, cause uncertain.

3 ADRs are classified as Type A (Augmented), B (Bizarre), C (Chronic), D (Delayed), E (End of use), F (Failure of therapy).

4 Type A is dose-related, predictable and common (~80%); Type B is not dose-related, unpredictable and often immune or genetic.

5 Main mechanisms: exaggerated pharmacological action, immune (allergic) attack, genetic (idiosyncratic) reactions, and drug interactions.

6 Risk factors fall into three groups: patient-related (age, sex, genes, pregnancy), disease-related (kidney/liver disease), and drug-related (polypharmacy, narrow therapeutic index, long duration).

7 Children, elderly, pregnant women and kidney/liver patients need extra caution.

Common confusions

1 **ADR vs ADE:** ADR means the drug is confirmed (or strongly suspected) as the cause at a normal dose. ADE only means something bad happened while on the drug — the drug may be innocent.

2 **Side effect vs ADR:** A side effect is an expected, accepted mild effect (drowsiness with antihistamine). An ADR is harmful and unwanted enough to matter clinically. In practice the terms overlap, but exams expect: side effect = expected/mild; ADR = harmful/unwanted.

3 **Allergy vs intolerance:** Allergy involves the immune system (antibodies, histamine) and can be life-threatening. Intolerance (e.g., stomach upset with a drug) does not involve the immune system and is usually milder.

4 **Type C vs Type D:** Type C appears during long-term continuous use (months–years of treatment). Type D appears after a delay — often long after the drug is stopped.

5 **Predictable does not mean prevented:** A predictable ADR (Type A) can still occur if monitoring is poor; predictability helps us watch for it, but prevention needs action.

Common mistakes

1 Thinking ADRs only happen with overdoses — by definition, ADRs happen at normal doses.

2 Calling every bad event during treatment an ADR without checking causality — it is an ADE until the drug link is assessed.

3 Mixing up Type A and Type B features in exams — remember: A = Augmented = dose-related/predictable; B = Bizarre = not dose-related/unpredictable.

4 Forgetting Type E (withdrawal) and Type F (therapy failure) — students often stop at A and B, but all six types are asked.

5 Re-prescribing a drug after a Type B allergic reaction — a Type B allergy means the drug must never be given again; this is a dangerous real-life error.

Mnemonics

- **Six ADR types — "A B C D E F" sentence:** "**A**unt **B**ina **C**ooks **D**inner **E**very **F**riday" — A=Augmented, B=Bizarre, C=Chronic, D=Delayed, E=End of use, F=Failure of therapy.
- **Type A vs B:** "**A** = **A**mount (dose matters); **B** = **B**olt from the blue (sudden, unpredictable)."
- **Risk factors — "KID PAGED": K**idney disease, **I**nfant/old age, **D**rugs many (polypharmacy), **P**regnancy, **A**llergy history, **G**enes, **E**xtra-long treatment (**D**uration).

Exam summary

Adverse drug reaction = harmful, unwanted effect at normal dose (WHO definition). ADE = bad event during drug use, cause uncertain. Six types: A-Augmented (dose-related, predictable, ~80%, e.g., bleeding with warfarin), B-Bizarre (not dose-related, unpredictable, immune/genetic, e.g., penicillin anaphylaxis), C-Chronic (long-term use, e.g., steroid cataract), D-Delayed (appears long after, even after stopping), E-End of use (withdrawal, e.g., rebound hypertension after clonidine), F-Failure of therapy (drug doesn't work, e.g., contraceptive failure with antibiotics). Mechanisms: exaggerated pharmacological action, immune attack, genetic/idiosyncratic reactions, drug interactions. Risk factors: patient (age extremes, sex, pregnancy, genes), disease (kidney/liver impairment), drug (polypharmacy, narrow therapeutic index, long duration, previous allergy).

One-minute revision

- ADR = harm at NORMAL dose; ADE = harm, cause unknown.
- A-Augmented, B-Bizarre, C-Chronic, D-Delayed, E-End of use, F-Failure.
- A: dose-related, predictable, common. B: not dose-related, unpredictable, immune/genetic.
- Mechanisms: too-strong drug action, allergy, genes, interactions.
- Risk: old/young age, pregnancy, kidney/liver disease, many drugs, previous allergy.
- Pharmacist = last safety checkpoint; counsel and report.

Questions

Short-answer questions

1 Define ADR as per WHO. How is it different from an adverse drug event (ADE)?

2 List the six types of ADRs with one example of each.

3 Differentiate between Type A and Type B adverse drug reactions (any four points).

4 What is an idiosyncratic reaction? Give one example with its genetic basis.

5 Name four patient-related risk factors for ADRs and explain any two.

6 What are Type E and Type F reactions? Give one example of each.

7 Why are elderly patients more prone to ADRs? Give two physiological reasons.

Long-answer questions

1 Classify adverse drug reactions. Describe each type in detail with suitable examples, and compare Type A and Type B reactions in a table.

2 Discuss the various mechanisms by which adverse drug reactions occur. Illustrate each mechanism with a suitable example and a flowchart.

3 Describe the risk factors for ADRs under the headings: patient-related, disease-related and drug-related factors. Explain why special populations (children, elderly, pregnant women, kidney/liver patients) need extra caution.

MCQs (with answer keys)

1 Which of the following best defines an adverse drug reaction?

a) Any harmful effect of a drug taken in overdose b) A harmful, unwanted effect of a drug at a normal therapeutic dose c) Any bad event occurring during drug therapy, cause unknown d) A beneficial effect of a drug other than the intended one **Answer: b**

1 Type A adverse drug reactions are characterised by all of the following EXCEPT:

a) Dose-related b) Predictable from the drug's pharmacology c) Uncommon, occurring in less than 5% of ADRs d) Managed by dose reduction **Answer: c**

1 Anaphylaxis following penicillin administration is an example of:

a) Type A reaction b) Type B reaction c) Type C reaction d) Type E reaction **Answer: b**

1 Rebound hypertension after sudden withdrawal of clonidine is classified as:

a) Type C reaction b) Type D reaction c) Type E reaction d) Type F reaction **Answer: c**

1 Which of the following is a patient-related risk factor for ADRs?

a) Polypharmacy b) Narrow therapeutic index c) Genetic G6PD deficiency d) Long duration of therapy **Answer: c**

1 Haemolysis caused by primaquine in G6PD-deficient individuals is an example of:

a) Pharmacological mechanism b) Immunological mechanism c) Idiosyncratic mechanism d) Drug interaction mechanism **Answer: c**

1 Contraceptive failure due to an interacting antibiotic is an example of:

a) Type D reaction b) Type E reaction c) Type F reaction d) Type B reaction **Answer: c**

1 Which organ toxicity is correctly matched?

a) Ototoxicity — kidney damage b) Nephrotoxicity — liver damage c) Hepatotoxicity — liver damage d) Cardiotoxicity — ear damage **Answer: c**

1 A severe, life-threatening ADR that needs hospitalisation is classified by severity as:

a) Mild b) Moderate c) Severe d) Predictable **Answer: c**

1 Which statement about Type B reactions is TRUE?

a) They are dose-related and predictable b) They account for about 80% of all ADRs c) They are often immune-mediated or genetic and not dose-related d) They can be managed by simply reducing the dose **Answer: c**

Viva questions

1 What is the WHO definition of an adverse drug reaction?

2 Name the six types of ADRs.

3 Give one example each of Type A and Type B reactions.

4 What is the difference between a side effect and an ADR?

5 Why should a drug that caused a Type B allergic reaction never be given again?

6 Name three risk factors that make elderly patients prone to ADRs.

Application-based questions

1 A patient develops a widespread skin rash with blisters two weeks after starting carbamazepine for epilepsy. Classify the ADR by type and severity, explain the likely mechanism, and state the immediate management step and the pharmacist's counselling points for future prescriptions.

2 A 68-year-old woman with liver disease is prescribed a normal adult dose of a drug that is mainly broken down by the liver. Predict the ADR risk, name the type of reaction most likely, and suggest what the prescriber and pharmacist should do.

References

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CHAPTER 9: ADR Monitoring, Assessment and Management

Learning Objectives

After studying this chapter, the student should be able to:

1 List the methods of ADR monitoring and describe spontaneous reporting in detail.

2 Explain cohort studies and case-control studies as used in pharmacovigilance.

3 Describe how ADRs are detected — clinical observation, laboratory tests and patient reporting.

4 Explain the steps in reporting an ADR and the contents of a good ADR report.

5 Define and describe causality assessment, and name the commonly used tools conceptually.

6 Define and describe severity, predictability and preventability assessment of ADRs.

7 Outline the steps in the management of a patient who develops an ADR.

Definitions

ADR monitoring. ADR monitoring means the continuous, organised watching for unwanted harmful effects of medicines in patients — by doctors, pharmacists, nurses and patients themselves — so that reactions are found early and harm is reduced.

ADR detection. ADR detection is the process of recognising that an unwanted event in a patient is actually caused by a medicine. Detection is the "finding" step; reporting is the "telling" step.

ADR reporting. ADR reporting is the formal communication of a suspected adverse drug reaction, with patient and drug details, to an ADR Monitoring Centre or the national pharmacovigilance programme.

Spontaneous reporting. Spontaneous reporting is the voluntary reporting of a suspected ADR by a health professional or patient, on their own initiative, without being asked or being part of a study. It is the backbone of pharmacovigilance worldwide.

Causality assessment. Causality assessment is the structured judgement of how likely it is that a particular drug actually caused the observed reaction — in other words, answering "did this drug really do this?"

Severity assessment. Severity assessment grades how serious or harmful the ADR was — mild, moderate or severe — based on the harm caused and the treatment needed.

Predictability assessment. Predictability assessment asks whether the ADR could have been expected from the drug's known properties.

Preventability assessment. Preventability assessment asks whether the ADR could have been avoided by better prescribing, dispensing, monitoring or patient education.

Management of ADRs. Management of ADRs means all the steps taken to treat the reaction, protect the patient, and prevent it from happening again.

Terminology table

Term	Simple meaning
Monitoring	Continuous watching for ADRs in patients
Detection	Recognising that a drug caused the unwanted event

Term	Simple meaning
Reporting	Formally informing the pharmacovigilance system about the ADR
Spontaneous reporting	Voluntary, on-your-own reporting of a suspected ADR
Cohort study	Following a group of drug users over time to see what ADRs appear
Case-control study	Comparing patients with an ADR (cases) to patients without it (controls) to find the cause
Dechallenge	Stopping the suspected drug and watching whether the reaction goes away
Rechallenge	Giving the suspected drug again to see whether the reaction returns (done only when safe)
Causality	How likely the drug caused the reaction (certain, probable, possible, unlikely)
Severity	How harmful the reaction was (mild, moderate, severe)
Signal	New information suggesting a previously unknown drug–ADR link
Reporter	The person (doctor, pharmacist, nurse, patient) who reports the ADR
Serious ADR	An ADR causing death, hospitalisation, disability, birth defect or life threat
Medication error	A preventable mistake in prescribing, dispensing or taking a medicine

Simple explanations

Why monitor ADRs after a drug is approved? Before approval, a drug is tested in only a few thousand people for a short time. Rare reactions, reactions in special groups (pregnant women, children, elderly), and reactions from long-term use or drug interactions only appear when lakhs of people use the drug for years. Monitoring after marketing catches what trials missed.

What is spontaneous reporting, simply? A doctor notices a strange rash after a new tablet and reports it voluntarily — nobody asked. Thousands of such reports, collected together, reveal patterns. One report is a hint; a hundred on the same drug prove the problem.

What is causality assessment, simply? A patient on five medicines develops liver damage. Which medicine did it — or was it the disease itself? Causality assessment is a step-by-step method to weigh the evidence and grade the link: certain, probable, possible, or unlikely.

What does management of an ADR mean, simply? First stop the harm (stop or change the drug), then treat the damage (antidote, supportive care), then make sure it never happens again (record the allergy, counsel the patient, inform the doctor, report the ADR).

Classifications

Methods of ADR monitoring (pharmacovigilance data collection methods)

Method	How it works (simple)	Strengths	Limitations
Spontaneous reporting	Health workers/patients voluntarily report suspected ADRs	Cheap; covers the whole population; finds rare and new reactions	Under-reporting; incomplete information; cannot calculate exact rates
Cohort studies	A group taking the drug is followed over time; ADRs are counted	Can calculate incidence; studies large numbers	Expensive; slow; needs large groups for rare ADRs
Case-control studies	Patients with the ADR (cases) are compared with similar patients without it (controls)	Good for rare ADRs; quick and cheap	Recall bias; cannot calculate incidence directly
Intensive hospital monitoring	Trained staff watch every patient in selected wards for ADRs	Very complete data	Expensive; limited to a few hospitals
Prescription event monitoring	Prescriptions are tracked and doctors are asked about events in those patients	Good denominator data	Depends on doctor response
Patient/consumer reporting	Patients report their own suspected ADRs directly	Adds the patient's own experience; increases reports	May lack medical detail

Mechanisms and processes — how reports become a signal (signal-generation process)

Technical concept: A single ADR report is only a suspicion. When many similar reports accumulate in a database, statistical and clinical review may identify a "signal" — a new possible drug–ADR link needing investigation.

Simple explanation: One person shouting "fire" might be mistaken. Fifty people shouting "fire" from the same building means there really is a fire. The process is: reports accumulate → pattern noticed → experts review → signal confirmed or rejected → action taken.

```
Individual reports accumulate in the database
        |
        v
Unusual pattern noticed (more reports than expected)
        |
        v
Clinical review: are the cases similar? Is timing right?
Are other causes ruled out?
        |
        v
Signal confirmed → regulatory action
        |
        v
Signal rejected → continued routine monitoring
```

Key takeaway: Monitoring is a funnel — thousands of reports go in, and only validated signals come out as safety action.

Detection of ADRs — how reactions are found

1. **Clinical observation:** The doctor, nurse or pharmacist notices new symptoms after a drug is started (rash, swelling, jaundice, bleeding).
2. **Laboratory tests:** Blood tests reveal hidden harm — raised liver enzymes, low white blood cells, raised creatinine (kidney harm).

3 **Patient complaints:** The patient reports dizziness, nausea or itching that began with the new medicine.

4 **Review of medical records:** Looking back at patient files to find patterns of harm linked to a drug.

5 **Literature and signal review:** Published case reports and database patterns that point to new drug–ADR links.

Steps in ADR reporting (the reporting process)

```
Suspected ADR noticed by doctor / pharmacist / nurse / patient
        |
        v
Collect details: patient, drug(s), reaction, dates, outcome
        |
        v
Fill the ADR reporting form (as per the latest guidelines/notifications
– confirm the current edition)
        |
        v
Send to the nearest ADR Monitoring Centre (AMC)
        |
        v
AMC checks quality, assesses causality, enters data
        |
        v
Data flows to the national centre (PvPI, IPC Ghaziabad)
        |
        v
Serious/unexpected signals shared with WHO (VigiBase)
        |
        v
Regulatory action if needed (label change, warning, restriction)
```

Contents of a good ADR report

- Patient details: age, sex, weight (no name needed — privacy is protected)
- Suspected drug(s): name, dose, route, dates started and stopped, reason for use
- Reaction details: what happened, when it started, how severe, treatment given, outcome (recovered / recovering / not recovered / fatal)
- Other drugs the patient was taking (to check interactions)
- Medical history and allergies
- Dechallenge/rechallenge information (did the reaction stop when the drug was stopped?)
- Reporter details: name, contact, profession

Assessment of ADRs — four assessments

1. Causality assessment. The question: did the drug cause this reaction? The evidence is weighed using factors such as: timing (did the reaction start after the drug?), dechallenge (did it improve when the drug was stopped?), rechallenge (did it return if the drug was restarted — done only when safe), alternative causes (could the disease or another drug explain it?), and known pattern (is this reaction already known with this drug?). Based on this, the link is graded in categories such as certain, probable, possible or

unlikely. Two well-known structured tools are the **Naranjo scale** (a questionnaire-based scoring approach) and the **WHO-UMC causality assessment system** (the WHO's standardised method) — both are described here conceptually, without inventing score cut-offs or versions, as per the latest guidelines/notifications.

2. Severity assessment. The question: how bad was it? Commonly graded as mild (no treatment needed), moderate (needed treatment or dose change) or severe (life-threatening, hospitalisation, permanent harm or death). Structured scales exist (for example, the Hartwig severity scale is a well-known graded approach) — described conceptually here; confirm the current edition as per the latest guidelines.

3. Predictability assessment. The question: could this have been expected? A reaction is predictable if it is a known effect of the drug's pharmacology (Type A). It is unpredictable if it was unknown or idiosyncratic (Type B).

4. Preventability assessment. The question: could this have been avoided? Structured approaches (such as the Schumock and Thornton preventability criteria, a well-known framework) ask whether the drug was wrong for the patient, the dose was wrong, monitoring was missing, a known allergy was ignored, or a drug interaction was missed. If yes to such questions, the ADR was preventable. Described conceptually; confirm the current edition as per the latest guidelines.

Comparison table: the four assessments

Assessment	Question it answers	Example conclusion
Causality	Did the drug cause it?	"Probable — reaction followed the drug, improved on stopping, no other cause found"
Severity	How bad was it?	"Moderate — needed antihistamine treatment and drug change"
Predictability	Could it have been expected?	"Predictable — known side effect of this drug class"
Preventability	Could it have been avoided?	"Preventable — patient's known allergy was not checked"

Management of ADRs — stepwise approach

```
Step 1: RECOGNISE — identify the reaction and the suspected drug
        |
        v
Step 2: STOP or CHANGE — stop the suspected drug (immediately if severe/allergic);
        substitute a safer alternative if treatment must continue
        |
        v
Step 3: TREAT the reaction — antidote if available (e.g., antihistamine for allergy,
        vitamin K for warfarin bleeding); supportive care (fluids, oxygen)
        |
        v
Step 4: MONITOR — watch until the patient fully recovers; check lab values
        |
        v
Step 5: DOCUMENT — record the ADR in the patient's file; issue an allergy card
        |
        v
Step 6: COUNSEL — tell the patient which drug caused it and to avoid it lifelong
        (especially for allergic/Type B reactions)
        |
        v
Step 7: REPORT — send the ADR report to the AMC (feeds national and global safety data)
```

Key takeaway: Management is not only treating the patient in front of you — steps 5, 6 and 7 protect the same patient in the future and protect thousands of other patients through the reporting system.

Infographic concept box

INFOGRAPHIC CONCEPT: "From Suspicion to Safety — the ADR journey." A left-to-right pipeline with seven stations: 1) EYE (Detect — clinician spots the reaction), 2) FORM (Report — filled ADR form), 3) BUILDING (AMC — monitoring centre verifies), 4) MAP OF INDIA (PvPI national centre collates), 5) GLOBE (WHO VigiBase — global data), 6) MAGNIFYING GLASS (Assess — causality, severity, predictability, preventability judged), 7) SHIELD (Act — label change, warning, or drug restriction). Above the pipeline, four assessment badges: "Did the drug do it?" (causality), "How bad?" (severity), "Expected?" (predictability), "Avoidable?" (preventability). Bottom banner: "One report can protect a million patients — report every suspected ADR."

Tables

Table: Spontaneous reporting vs cohort studies vs case-control studies

Feature	Spontaneous reporting	Cohort study	Case-control study
Design	Voluntary reports, no fixed plan	Follow drug users forward in time	Compare ADR cases with controls, looking backward
Best for	Finding new, rare signals	Measuring how often ADRs occur	Studying rare ADRs quickly
Cost	Low	High	Low–moderate
Main weakness	Under-reporting	Expensive and slow	Recall bias; no incidence rate

Feature	Spontaneous reporting	Cohort study	Case-control study
Example use	First hint of a new rash with a new drug	10,000 patients on a new diabetes drug followed for 2 years	50 liver-injury cases vs 100 controls to test a drug link

Table: Serious ADR criteria (when an ADR counts as "serious")

Criterion	Simple meaning
Death	The reaction caused or contributed to death
Life-threatening	The patient was at immediate risk of dying
Hospitalisation	Needed admission, or stay got longer
Disability	Lasting damage to body function
Congenital anomaly	Birth defect in a baby exposed in the womb
Medically important event	A doctor judges it serious even if none of the above apply

Any serious ADR must be reported on priority — as per the latest guidelines/notifications, confirm the current reporting timelines.

Examples

1. **Spontaneous reporting:** A pharmacist notices three patients developing a persistent cough after starting the same blood pressure medicine (an ACE inhibitor). Each report alone is a hint; together at the AMC they confirm a known Type A pattern.
2. **Cohort study:** 5,000 patients starting a new cholesterol drug are followed for one year; 40 develop muscle pain — the study measures incidence.
3. **Causality:** A patient develops jaundice 10 days after starting anti-tubercular treatment; it fades when the drugs are stopped (positive dechallenge); no alcohol use or viral hepatitis found. Causality: probable drug-induced liver injury.
4. **Management:** A patient on warfarin shows bleeding gums and a very high INR. Management: stop warfarin, give vitamin K (antidote), monitor INR, restart later at a lower dose with closer monitoring, counsel the patient, and report the ADR.

Analogies

1. **Spontaneous reporting — the neighbourhood watch:** One neighbour reporting a broken streetlight is a hint; fifty neighbours reporting the same dark street proves the problem. Each voluntary report is one neighbour speaking up.
2. **Causality assessment — the detective:** A detective checks the timeline, the motive (does the drug's action explain it?) and alibis (could the disease or another drug have done it?). Causality assessment is detective work for ADRs.
3. **Dechallenge/rechallenge — the light switch:** Switch off the light (stop the drug) — does the room go dark (reaction fades)? Switch it on again (restart, only if safe) — does the light return? That is dechallenge and rechallenge.

Pharmacy relevance

- Pharmacists are among the most active ADR reporters: they see the prescription, know the patient's other medicines, and are often the first to hear patient complaints.
- Every pharmacy attached to a hospital can function with or support an ADR Monitoring Centre; pharmacists verify report quality, assess causality, and enter data.
- While dispensing, the pharmacist applies preventability thinking in real time — checking allergies, doses, interactions and duplicate therapies before the medicine leaves the counter.
- Pharmacist-led patient counselling ("this medicine may cause dizziness — report it, don't just stop the drug") improves both detection and reporting.
- In management, the pharmacist suggests safer alternative drugs, checks antidote availability, and issues allergy documentation so the reaction is never repeated.

India context

- The Pharmacovigilance Programme of India (PvPI) is coordinated by the Indian Pharmacopoeia Commission (IPC), Ghaziabad, with ADR Monitoring Centres in medical colleges and hospitals across the country — as per the latest guidelines/notifications, confirm the current edition for the reporting form and timelines.
- PvPI provides a toll-free helpline and mobile app–based reporting options for health professionals and consumers — confirm current contact details as per the latest notifications.
- Under-reporting is a recognised challenge in India: busy clinics, lack of awareness, and the belief that "only new or serious reactions need reporting" reduce report numbers. Every suspected ADR is worth reporting because Indian population data matters.
- Anti-tubercular drugs, antibiotics and antiepileptics are among the frequently reported ADR sources in Indian AMCs, reflecting national disease patterns.

Key points

1. ADR monitoring methods: spontaneous reporting (main method), cohort studies, case-control studies, intensive hospital monitoring, prescription event monitoring, patient reporting.
2. Spontaneous reporting is voluntary, cheap and population-wide, but suffers from under-reporting.
3. Detection happens through clinical observation, lab tests, patient complaints and record review.
4. A good ADR report contains patient details, drug details, reaction details, dates, outcome, other drugs, history, and dechallenge/rechallenge information.
5. Four assessments: causality (did the drug cause it?), severity (how bad?), predictability (expected?), preventability (avoidable?).
6. Causality tools include the Naranjo scale and WHO-UMC system (conceptual description; confirm current edition as per latest guidelines).
7. Management steps: recognise → stop/change drug → treat reaction → monitor → document → counsel → report.

Common confusions

1. **Monitoring vs detection vs reporting:** Monitoring is continuous watching; detection is recognising the drug caused it; reporting is formally informing the system. They are three steps in order.
2. **Causality vs severity:** Causality asks "did the drug do it?"; severity asks "how bad was it?" A certain causality can pair with mild severity, and vice versa.
3. **Spontaneous reporting vs cohort study:** Spontaneous reporting is voluntary and unplanned (finds signals); a cohort study is a planned research study following patients over time (measures rates).
4. **Dechallenge vs rechallenge:** Dechallenge = stop the drug, watch improvement. Rechallenge = restart the drug, watch return. Rechallenge is often unethical/unsafe and is not required for a report.
5. **Serious vs severe:** "Serious" is a regulatory term with fixed criteria (death, hospitalisation, disability, etc.). "Severe" describes intensity. A severe headache is not automatically a "serious" ADR unless it meets the criteria.

Common mistakes

1. Not reporting because "the reaction is already well known" — known reactions still need reporting; they build Indian population data and detect changes in frequency.
2. Reporting only the drug name without dates, doses and outcome — an incomplete report cannot be assessed for causality.
3. Attempting rechallenge in a serious allergic reaction just to "confirm" causality — dangerous and unnecessary.
4. Confusing preventability with predictability — a predictable ADR (expected from pharmacology) can still be unpreventable, and an unpredictable one is rarely preventable.
5. Forgetting to document the ADR in the patient's own record and counsel the patient — the system report alone does not protect that patient next time.
6. Delaying serious ADR reports — serious reactions need priority reporting as per the latest guidelines/notifications.

Mnemonics

- **Monitoring methods — "SCCIPP":** "**S**pontaneous reporting, **C**ohort, **C**ase-control, **I**ntensive monitoring, **P**rescription event monitoring, **P**atient reporting."
- **Four assessments — "Can Sally Predict Prevention":** **C**ausality, **S**everity, **P**redictability, **P**reventability.
- **Good report contents — "P-DROP":** **P**atient, **D**rug, **R**eaction, **O**utcome, **P**lus history/reporter.

Exam summary

ADR monitoring = continuous organised watching for drug harms. Main methods: spontaneous reporting (voluntary, backbone of pharmacovigilance, but under-reported), cohort studies (follow users forward, give incidence), case-control studies (compare cases with controls, good for rare ADRs), intensive hospital monitoring, prescription event monitoring, patient reporting. Detection via clinical observation, lab tests, patient complaints, record review. Reporting flow: suspicion → collect details → fill ADR form → AMC → PvPI (IPC Ghaziabad) → WHO VigiBase → regulatory action. Good report: patient, drug, reaction, dates, outcome, other drugs, history, dechallenge/rechallenge, reporter. Four assessments: causality (did the drug cause it — Naranjo scale, WHO-UMC system, conceptual), severity (mild/moderate/severe), predictability (expected or not), preventability (avoidable or not — e.g., Schumock and Thornton framework, conceptual). Serious ADR criteria: death, life threat, hospitalisation, disability, birth defect, medically important. Management: recognise → stop/change drug → treat (antidote/supportive) → monitor → document → counsel → report.

One-minute revision

- Monitor = watch; detect = recognise; report = inform.
- Main method: spontaneous (voluntary) reporting.
- Cohort = forward, gives rates; case-control = backward, good for rare ADRs.
- Report: patient, drug, reaction, dates, outcome, reporter → AMC → PvPI → WHO.
- 4 assessments: causality, severity, predictability, preventability.
- Manage: recognise, stop, treat, monitor, document, counsel, report.

Questions

Short-answer questions

1 What is spontaneous reporting? List two strengths and two limitations.

2 Differentiate between cohort studies and case-control studies in pharmacovigilance.

3 What are the contents of a good ADR report?

4 Define causality assessment. What factors are considered while judging causality?

5 List the criteria that make an ADR "serious" as per regulatory definition.

6 Outline the steps in the management of a patient with a suspected ADR.

Long-answer questions

1 Describe the various methods of ADR monitoring. Compare spontaneous reporting, cohort studies and case-control studies with respect to design, strengths and limitations.

2 Explain the process of ADR detection and reporting in India, from the bedside to the WHO database, with a flowchart. What makes a good ADR report?

3 Discuss the four assessments applied to an ADR — causality, severity, predictability and preventability — giving the key question, approach and an example for each.

MCQs (with answer keys)

1 The backbone of pharmacovigilance worldwide is:

a) Cohort studies b) Spontaneous reporting c) Case-control studies d) Animal testing **Answer: b**

1 Which study design follows a group of drug users forward in time to measure ADR incidence?

a) Case-control study b) Cross-sectional study c) Cohort study d) Case report **Answer: c**

1 A case-control study is particularly useful for:

a) Measuring the exact incidence of common ADRs b) Studying rare ADRs quickly and cheaply c) Replacing spontaneous reporting d) Testing drugs before approval **Answer: b**

1 Improvement of the reaction after stopping the suspected drug is called:

a) Rechallenge b) Dechallenge c) Causality d) Signal **Answer: b**

1 Which of the following is NOT a criterion for a "serious" ADR?

a) Death b) Hospitalisation c) Mild nausea not needing treatment d) Congenital anomaly **Answer: c**

1 Causality assessment primarily answers the question:

a) How bad was the reaction? b) Did the drug cause the reaction? c) Could the reaction have been expected? d) Could the reaction have been avoided? **Answer: b**

1 Preventability assessment asks:

a) Whether the drug caused the reaction b) Whether the reaction could have been avoided by better care c) How severe the reaction was d) Whether the reaction is listed in the product label **Answer: b**

1 The first step in managing a patient with a suspected serious ADR is to:

a) Report to the WHO immediately b) Recognise the reaction and stop/change the suspected drug c) Rechallenge with the same drug d) Wait for laboratory confirmation before acting **Answer: b**

1 A well-known structured questionnaire-based tool for causality assessment is:

a) The Naranjo scale b) The Hartwig scale c) The Schumock and Thornton criteria d) The CIOMS form **Answer: a**

1 In India, ADR reports from AMCs are collated nationally by:

a) CDSCO directly from patients b) The Pharmacovigilance Programme of India, coordinated by IPC Ghaziabad c) The Indian Medical Association d) The WHO country office alone **Answer: b**

Viva questions

1 Define spontaneous reporting.

2 Name three methods of ADR monitoring besides spontaneous reporting.

3 What is the difference between a cohort study and a case-control study?

4 What four assessments are applied to a reported ADR?

5 What is dechallenge? What is rechallenge?

6 List any three criteria of a serious ADR.

Application-based questions

1 You are a hospital pharmacist. A nurse tells you a patient developed sudden swelling of the face and difficulty breathing 20 minutes after an IV antibiotic. List your immediate management steps, the assessments you would perform, and how you would complete the reporting chain.

2 An elderly patient is readmitted with bleeding while on warfarin plus an NSAID started by another doctor. Assess preventability, identify the errors in the medication process, and suggest system-level measures the pharmacy can implement to prevent recurrence.

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CHAPTER 10: Online Reporting Mechanisms, Databases and MedDRA

Learning Objectives

After studying this chapter, the student should be able to:

1 Name the major online ADR reporting mechanisms and databases used in pharmacovigilance.

2 Explain the purpose and basic working of WHO-ART, VigiBase, VigiFlow, Oracle Argus and OpenVigil.

3 Compare VigiBase, VigiFlow and OpenVigil in a table.

4 Compare WHO-ART and MedDRA in a table.

5 Define MedDRA and describe its hierarchical structure (SOC, HLGT, HLT, PT, LLT) in simple words.

6 Explain why standardised medical terminology (coding dictionaries) is essential in pharmacovigilance.

7 Describe how a pharmacist uses these tools in ADR reporting practice.

Definitions

Online reporting mechanism. An online reporting mechanism is a website, portal or software through which a suspected ADR can be reported electronically instead of on paper — faster, searchable and directly entering databases.

Database (in pharmacovigilance). A pharmacovigilance database is a large, organised electronic store of ADR reports collected from many sources, used to find patterns and safety signals.

WHO-ART. WHO-ART (WHO Adverse Reaction Terminology) is the World Health Organization's older standardised dictionary of terms used to code (label) adverse drug reactions in reports.

VigiBase. VigiBase is the WHO's global database of individual case safety reports — the world's largest collection of ADR reports, maintained by the Uppsala Monitoring Centre (UMC) in Sweden.

VigiFlow. VigiFlow is the WHO–UMC's web-based system that national pharmacovigilance centres use to enter, manage and send ADR reports to VigiBase.

Oracle Argus. Oracle Argus is a commercial (paid) drug-safety software used by pharmaceutical companies and regulators to collect, process and report adverse events and meet regulatory timelines.

OpenVigil. OpenVigil is a free, open-access tool that lets anyone search and analyse publicly available ADR data (mainly from the US FDA's database) without needing special software.

MedDRA. MedDRA (Medical Dictionary for Regulatory Activities) is the international standard medical terminology dictionary used to code adverse events in drug regulation and pharmacovigilance.

Coding (of ADRs). Coding means converting the reporter's own words (e.g., "patient felt dizzy") into a standard dictionary term (e.g., "Dizziness") so that computers can count and compare reports worldwide.

Terminology table

Term	Simple meaning
Individual Case Safety Report (ICSR)	A single structured ADR report about one patient at one point in time
Uppsala Monitoring Centre (UMC)	The WHO centre in Sweden that runs the global drug-monitoring programme
Signal detection	Using database data to find new, previously unknown drug–ADR links
Data mining	Computer searching of huge databases for hidden patterns
Coding dictionary	A standard list of medical terms used to label ADRs uniformly
Preferred Term (PT)	MedDRA's single standard name for one medical concept
Lowest Level Term (LLT)	MedDRA's most detailed, everyday-word term (e.g., "feeling queasy")
System Organ Class (SOC)	MedDRA's top level — the body system (e.g., heart, skin)
E2B	The international electronic format for sending ICSRs between systems
FAERS	The US FDA's adverse event database searched through tools like OpenVigil

Simple explanations

Why do we need online reporting? Paper forms are slow, get lost, and cannot be searched. Online reporting sends the ADR instantly to the monitoring centre, where it joins lakhs of other reports in a database that computers can analyse for patterns.

Why do we need databases like VigiBase? One hospital sees one case of a rare reaction — that proves nothing. But when 50 countries report the same rare reaction with the same drug into one global database, a safety signal appears. VigiBase is that one global collection point.

Why do we need coding dictionaries like MedDRA? A doctor in India writes "chakkar aana," a doctor in France writes "vertige," and a doctor in Brazil writes "tontura" — all meaning dizziness. Without a standard dictionary, the computer cannot recognise they are the same reaction. Coding converts all these words into one standard term so global counting works.

What is the difference between VigiBase, VigiFlow and OpenVigil? VigiBase is the big global storehouse of reports. VigiFlow is the entry door — the software national centres use to put reports into VigiBase. OpenVigil is a free public window to look at (mainly US) ADR data. Storehouse, door, window — three different jobs.

Classifications

The ADR data journey: from bedside to global database

```
Patient experiences suspected ADR
        |
        v
Reporter fills ADR form (paper or ONLINE portal)
        |
        v
ADR Monitoring Centre — report checked, coded (MedDRA/WHO-ART),
causality assessed
        |
        v
National centre (PvPI, IPC Ghaziabad) — data entered via VigiFlow
        |
        v
VigiBase (WHO global database, Uppsala Monitoring Centre)
        |
        v
Signal detection by data mining → safety signal
        |
        v
Regulatory action (warning, label change, restriction)
```

MedDRA hierarchy — five levels, top to bottom

```
Level 1: System Organ Class (SOC) — the body system
            e.g., "Cardiac disorders"
                |
Level 2: High Level Group Term (HLGT) — group of related conditions
            e.g., "Cardiac arrhythmias"
                |
Level 3: High Level Term (HLT) — more specific group
            e.g., "Supraventricular arrhythmias"
                |
Level 4: Preferred Term (PT) — ONE standard name for the concept
            e.g., "Atrial fibrillation"
                |
Level 5: Lowest Level Term (LLT) — reporter's everyday wording
            e.g., "Auricular fibrillation"
```

Simple explanation of the ladder: Imagine a library. SOC is the floor (which body system). HLGT and HLT are the shelves and rows. PT is the exact book title — one official name. LLT is the nickname people use when asking for the book. The librarian (coder) always files it under the official title (PT).

Key takeaway: Every ADR report is coded up this ladder so that a "chakkar" in India and "dizziness" in the UK are counted as the same reaction worldwide.

Classification of the tools by user

Tool	Main user	Job
Online reporting portals/apps	Doctors, pharmacists, patients	Submit the ADR quickly
VigiFlow	National pharmacovigilance centres	Enter and manage national reports; send to VigiBase
VigiBase	WHO/UMC, regulators, researchers	Store and analyse global reports; signal detection
Oracle Argus	Pharmaceutical companies, regulators	End-to-end company drug-safety processing and regulatory reporting
OpenVigil	Students, researchers, public	Free searching of public ADR data
MedDRA / WHO-ART	Coders at AMCs and companies	Standard words for labelling reactions

Infographic concept box

INFOGRAPHIC CONCEPT: "The Global ADR Highway." A world map with three lanes. Lane 1 — "REPORT": icons of a doctor, pharmacist and patient sending forms into a laptop labelled "Online reporting portal." Lane 2 — "COLLECT": national centres shown as buildings feeding reports through a pipe labelled "VigiFlow" into a giant global cylinder labelled "VigiBase — lakhs of reports, 150+ countries." Lane 3 — "UNDERSTAND": the giant cylinder connects to a magnifying glass ("Signal detection") and a dictionary book ("MedDRA — one language for ADRs"). A side panel compares "WHO-ART (older WHO dictionary)" vs "MedDRA (current international standard)" as two book covers, old vs new. Bottom banner: "Same reaction, same word, worldwide — that is why coding matters."

Tables

Table: VigiBase vs VigiFlow vs OpenVigil (comparison)

Feature	VigiBase	VigiFlow	OpenVigil
What it is	WHO global ADR database	WHO web-based reporting/management system	Free open-access data search tool
Maintained by	Uppsala Monitoring Centre (UMC), Sweden	WHO–UMC	Independent/open-access initiative
Main users	Regulators, WHO, researchers	National pharmacovigilance centres	Students, researchers, public
Purpose	Store worldwide ICSRs; signal detection	Enter, manage and transmit national reports to VigiBase	Search and analyse public ADR data (mainly US FDA data)

Feature	VigiBase	VigiFlow	OpenVigil
Access	Restricted to authorised centres/regulators	Authorised national centre staff	Free and open to anyone
Cost	Part of WHO programme infrastructure	Provided through WHO programme	Free

Table: WHO-ART vs MedDRA (comparison)

Feature	WHO-ART	MedDRA
Full form	WHO Adverse Reaction Terminology	Medical Dictionary for Regulatory Activities
Developed by	World Health Organization	International Council for Harmonisation (ICH) process
Status	Older terminology, historically used in WHO programme	Current international standard for regulatory use
Structure	Hierarchical but simpler	Five-level hierarchy (SOC → HLGT → HLT → PT → LLT)
Use today	Legacy data; largely replaced for new coding	Used by regulators and industry worldwide for coding adverse events
Key takeaway	The earlier common language	The present common language

Table: MedDRA hierarchy at a glance

Level	Name	What it is (simple)	Example
1 (top)	System Organ Class (SOC)	Body system	Cardiac disorders
2	High Level Group Term (HLGT)	Group of related conditions	Cardiac arrhythmias
3	High Level Term (HLT)	Narrower group	Supraventricular arrhythmias
4	Preferred Term (PT)	Single official name	Atrial fibrillation
5 (bottom)	Lowest Level Term (LLT)	Everyday wording	Auricular fibrillation

Mnemonic for the ladder: "**S**ome **H**ospitals **H**ave **P**retty **L**obbies" — **S**OC, **H**LGT, **H**LT, **P**T, **L**LT.

Examples

1. **Coding example:** A reporter writes "patient complained of chakkar after the tablet." The coder maps this to the standard term "Dizziness" (a Preferred Term) under the SOC "Nervous system disorders." Now it can be counted with all dizziness reports worldwide.
2. **VigiFlow example:** An AMC in a medical college assesses an ADR, codes it, and enters it into VigiFlow; the national centre reviews it and it flows onward to VigiBase.
3. **VigiBase signal example (conceptual):** Reports of the same rare skin reaction with a new drug arrive from several countries into VigiBase; data mining flags the pattern as a signal for expert review — no invented numbers or dates are used here.
4. **Oracle Argus example:** A pharmaceutical company receives a serious ADR report from a clinical trial; its drug-safety team processes it in Oracle Argus and submits it to regulators within required timelines — as per the latest guidelines/notifications, confirm the current edition.

5 **OpenVigil example:** A pharmacy student wants to know which ADRs are most commonly reported with a particular antibiotic in the US FDA data; OpenVigil lets her search and view the pattern free of cost.

6 **MedDRA ladder example:** "Itchy red rash" (LLT wording) → coded to PT "Rash" → under HLT/HLGT skin groups → SOC "Skin and subcutaneous tissue disorders."

Analogies

1 **VigiBase — the world library:** Every country sends its ADR "books" to one world library. One book proves little, but when fifty books describe the same problem, the librarians (safety scientists) know something real is happening.

2 **VigiFlow — the post office:** You write a letter (ADR report) and drop it at the post office (VigiFlow); the postal system delivers it to the world library (VigiBase). The post office is not the library — it is the delivery channel.

3 **MedDRA — one measuring scale:** If every shop used its own kilogram, trade would be chaos. MedDRA is the single standard "kilogram" for naming adverse reactions, so every country's reports can be weighed together.

4 **Coding — translating nicknames:** In a classroom, one student is called "Chintu" by friends, but the attendance register uses his official name. Coding is writing the official name (PT) in the register so the record is uniform.

Pharmacy relevance

- Pharmacists at AMCs do the coding: converting reporter language into MedDRA/WHO-ART terms is a core pharmacy skill in pharmacovigilance centres.
- Hospital and community pharmacists use online reporting portals to submit ADRs in minutes — knowing these mechanisms removes the "reporting is difficult" barrier.
- Understanding VigiBase and signal detection helps pharmacists appreciate why their single report matters: it joins a global pool that can change a drug's label worldwide.
- In industry, pharmacists work as drug-safety associates using tools like Oracle Argus to process cases and meet regulatory reporting timelines.
- Students can use OpenVigil for projects and dissertations to study real-world ADR patterns without needing restricted database access.

India context

- India's PvPI, coordinated by IPC Ghaziabad, uses VigiFlow to transmit Indian ADR reports to VigiBase — making India one of the contributing countries to the WHO global database.
- PvPI offers online and mobile-based ADR reporting for health professionals and consumers — as per the latest guidelines/notifications, confirm the current portal and app details before use.
- ADR Monitoring Centres in Indian medical colleges and hospitals are the ground-level users of these systems: they collect, code (using standard terminologies), assess and upload reports.

- Standardised coding matters especially in India because reports arrive in many languages and local wordings; MedDRA coding unifies them for global analysis.
- Indian pharmacy students should know these tools by name and function — questions on VigiBase, VigiFlow and MedDRA are frequently asked in pharmacovigilance examinations.

Key points

1 Online reporting mechanisms let reporters submit ADRs electronically — fast, searchable, and directly into databases.

2 VigiBase = WHO's global ADR database (Uppsala Monitoring Centre, Sweden); the world's largest collection of individual case safety reports.

3 VigiFlow = the WHO web system national centres use to enter and send reports to VigiBase.

4 Oracle Argus = commercial drug-safety software used by companies and regulators for case processing and regulatory reporting.

5 OpenVigil = free, open tool to search public ADR data (mainly US FDA data).

6 MedDRA = the current international standard dictionary for coding adverse events; five levels: SOC → HLGT → HLT → PT → LLT.

7 WHO-ART = the older WHO terminology, largely replaced by MedDRA for current coding.

8 Coding converts reporter wording into standard terms so global counting and signal detection work.

Common confusions

1 **VigiBase vs VigiFlow:** VigiBase is the database (the storehouse); VigiFlow is the software used to put reports into it (the entry door). They are not the same thing.

2 **WHO-ART vs MedDRA:** WHO-ART is the older WHO dictionary; MedDRA is the current international standard. Do not describe them as identical or interchangeable in current practice.

3 **OpenVigil vs VigiBase:** OpenVigil is a free public search tool (mainly US FDA data); VigiBase is the restricted WHO global database. OpenVigil does not give access to VigiBase.

4 **Oracle Argus vs VigiFlow:** Argus is commercial software mainly for pharmaceutical companies; VigiFlow is the WHO system for national centres. Different owners, different users.

5 **PT vs LLT:** The Preferred Term (PT) is the single official name used for counting; the Lowest Level Term (LLT) is the detailed everyday wording that gets mapped up to the PT.

6 **Reporting vs database:** Reporting is the act of sending an ADR; the database is where reports are stored. Online reporting mechanisms feed databases — they are linked steps, not synonyms.

Common mistakes

1 Writing that VigiBase is "a reporting website for patients" — it is a global database fed through national centres, not a public reporting portal.

2 Using WHO-ART and MedDRA as if they are the same dictionary — know which is older and which is the current standard.

3 Quoting invented version numbers, URLs or launch dates for these tools — as per the latest guidelines/notifications, confirm the current edition; never fabricate.

4 Forgetting the coder's role — students describe reporting but skip coding, yet coding (MedDRA) is what makes global analysis possible.

5 Mixing up the MedDRA hierarchy order — remember it goes from broad (SOC) to specific (LLT), with PT as the official counting term.

6 Thinking OpenVigil replaces formal reporting — it is a search/analysis tool, not a channel for submitting official ADR reports.

Mnemonics

- **The five tools — "Very Vigilant Officers Observe Meticulously": V**igiBase, **V**igiFlow, **O**racle Argus, **O**penVigil, **M**edDRA.
- **MedDRA ladder — "Some Hospitals Have Pretty Lobbies": S**OC → **H**LGT → **H**LT → **P**T → **L**LT.
- **Storehouse, door, window:** Vigi**B**ase = **B**ig storehouse; Vigi**F**low = **F**low of reports inward; **O**penVigil = **O**pen window for all.
- **WHO-ART vs MedDRA:** "**ART** is **art** history (older); **MedDRA** is the **modern** dictionary."

Exam summary

Online reporting mechanisms = electronic portals/software for submitting ADRs fast. Key databases and tools: VigiBase — WHO global database of individual case safety reports, maintained by the Uppsala Monitoring Centre, Sweden; world's largest ADR collection, used for signal detection. VigiFlow — WHO web-based system for national centres to enter, manage and transmit reports to VigiBase. Oracle Argus — commercial drug-safety software for pharmaceutical companies/regulators: case collection, processing and regulatory reporting. OpenVigil — free open-access tool to search public ADR data (mainly US FDA data). WHO-ART — older WHO adverse reaction terminology. MedDRA — Medical Dictionary for Regulatory Activities, the current international standard coding dictionary with five levels: System Organ Class (SOC) → High Level Group Term (HLGT) → High Level Term (HLT) → Preferred Term (PT) → Lowest Level Term (LLT). Coding converts reporter wording into standard terms so reactions can be counted and compared worldwide. Data journey: reporter → AMC (coding, causality) → national centre via VigiFlow → VigiBase → signal detection → regulatory action. India contributes through PvPI (IPC Ghaziabad) using VigiFlow.

One-minute revision

- VigiBase = WHO global ADR database (UMC, Sweden).
- VigiFlow = entry software for national centres → feeds VigiBase.
- Oracle Argus = company drug-safety software.
- OpenVigil = free public ADR data search.

- WHO-ART = older dictionary; MedDRA = current standard.
- MedDRA ladder: SOC → HLGT → HLT → PT → LLT.
- Coding = one standard word per reaction, worldwide.

Questions

Short-answer questions

1 What is VigiBase? Who maintains it and what is it used for?

2 Differentiate between VigiBase and VigiFlow.

3 What is Oracle Argus and who are its main users?

4 What is OpenVigil? How is it different from VigiBase?

5 Define MedDRA and list its five hierarchical levels in order.

6 Differentiate between a Preferred Term (PT) and a Lowest Level Term (LLT) with an example.

7 Compare WHO-ART and MedDRA (any four points).

8 Why is standardised coding of ADRs necessary? Explain with an example.

Long-answer questions

1 Describe the major online reporting mechanisms and databases used in pharmacovigilance: VigiBase, VigiFlow, Oracle Argus and OpenVigil. Compare them with respect to owner, users, purpose and access.

2 Explain MedDRA in detail: its purpose, five-level hierarchical structure with a labelled diagram, and the role of coding in global signal detection. Compare MedDRA with WHO-ART.

3 Trace the journey of an ADR report from a hospital bed in India to a global safety signal, describing the role of the AMC, PvPI, VigiFlow, VigiBase and MedDRA coding at each step, with a flowchart.

MCQs (with answer keys)

1 VigiBase is:

a) A commercial drug-safety software for companies b) The WHO global database of individual case safety reports c) A free public search tool for US FDA data d) An older WHO coding dictionary **Answer: b**

1 VigiBase is maintained by:

a) The US FDA b) The Uppsala Monitoring Centre (UMC), Sweden c) The Indian Pharmacopoeia Commission d) The European Medicines Agency **Answer: b**

1 The main function of VigiFlow is to:

a) Let the public search ADR data free of cost b) Allow national centres to enter, manage and transmit reports to VigiBase c) Process company clinical-trial safety cases d) Code ADRs using MedDRA automatically **Answer: b**

1 Oracle Argus is best described as:

a) A WHO reporting portal for patients b) Commercial drug-safety software used by pharmaceutical companies and regulators c) A free academic search engine d) The Indian national ADR database **Answer: b**

1 OpenVigil is:

a) The entry software for VigiBase b) A free, open-access tool to search public ADR data, mainly from the US FDA c) A coding dictionary d) A causality assessment scale **Answer: b**

1 MedDRA stands for:

a) Medical Dictionary for Regulatory Activities b) Medicines Database for Adverse Reaction Assessment c) Monitoring Database for Drug Reaction Analysis d) Medical Directory of Reported Adverse events **Answer: a**

1 In the MedDRA hierarchy, the level that gives the single official name for a medical concept is the:

a) System Organ Class (SOC) b) High Level Term (HLT) c) Preferred Term (PT) d) Lowest Level Term (LLT) **Answer: c**

1 The correct top-to-bottom order of the MedDRA hierarchy is:

a) LLT → PT → HLT → HLGT → SOC b) SOC → HLGT → HLT → PT → LLT c) PT → SOC → HLT → LLT → HLGT d) SOC → PT → LLT → HLT → HLGT **Answer: b**

1 WHO-ART differs from MedDRA in that WHO-ART is:

a) The current international standard b) The older WHO terminology, largely replaced by MedDRA c) A commercial software d) A global database **Answer: b**

1 Coding of ADRs using a standard dictionary is essential because it:

a) Increases the number of ADR reports b) Converts varied reporter wordings into uniform terms so reports can be counted and compared worldwide c) Replaces causality assessment d) Automatically treats the patient **Answer: b**

Viva questions

1 Expand VigiBase, VigiFlow and MedDRA.

2 Who maintains VigiBase?

3 What is the difference between VigiBase and VigiFlow in one line each?

4 Name the five levels of the MedDRA hierarchy.

5 What is a Preferred Term (PT)?

6 How is WHO-ART different from MedDRA?

7 What is OpenVigil used for?

8 Why do we code ADRs instead of using the reporter's own words?

Application-based questions

1 You are a pharmacist at an ADR Monitoring Centre. A doctor reports "patient felt chakkar and vomited twice after the new tablet." Describe how you would code this report using MedDRA levels, and explain each level you pass through.

2 A pharmaceutical company receives a serious ADR from its clinical trial. Which software system would its drug-safety team most likely use, and what steps would follow from case receipt to regulatory submission? (Answer conceptually, without inventing timelines.)

3 A researcher wants to study reporting patterns of antibiotic-associated diarrhoea using freely available data without institutional access. Which tool would you recommend, and what are its strengths and limitations for this purpose?

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