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B.PHARM 8th SEMESTER

BP805ET — PHARMACOVIGILANCE

UNIT — I • 10 Hours

Introduction • ADRs • Terminologies

PCI Syllabus • Exam-Focused • 25 MCQs • Question Bank

NTRODUCTION TO PHARMACOVIGILANCE

Definition (WHO, 2002)

> **📖 OFFICIAL WHO DEFINITION**
>
> **Pharmacovigilance** is defined by the WHO as ***"the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem."***

The word comes from two roots:

- ***Pharmakon*** (Greek) — drug/medicine
- ***Vigilare*** (Latin) — to keep watch

So literally pharmacovigilance means 'keeping watch on drugs'. It is NOT limited to side effects — it covers the entire safety profile of medicines throughout their lifecycle: clinical trials, marketing, post-marketing, and even withdrawal.

Aims & Objectives of Pharmacovigilance

As per WHO, the core aims of pharmacovigilance are:

1. Early detection of unknown adverse reactions and interactions.
2. Detection of increases in frequency of known adverse reactions.
3. Identification of risk factors and mechanisms underlying ADRs.
4. Estimation of quantitative aspects of benefit/risk analysis.
5. Dissemination of information to improve drug prescribing and regulation.
6. Promotion of rational and safe use of medicines.

> **MNEMONIC TIP**
>
> **Remember the 6 aims as "DDIIDP"** → Detect (unknown), Detect (frequency increase), Identify (risk factors), Investigate (benefit/risk), Disseminate (information), Promote (rational use).

Scope of Pharmacovigilance

Modern PV is not just about chemical drugs — its scope has expanded enormously and now includes:

Scope Area	Examples
Allopathic medicines	Antibiotics, cardiac drugs, antidiabetics
Herbal / AYUSH products	Ashwagandha, Triphala, Kadha (during COVID)
Biologicals & Vaccines	Insulin, Covishield, Covaxin, Hepatitis B vaccine
Blood products	Packed RBCs, platelets, plasma
Medical devices	Stents, IUDs, pacemakers
Traditional medicines	Siddha, Unani, Homeopathy
Drug interactions	Warfarin + aspirin → bleeding
Medication errors	Wrong dose, wrong route, wrong patient
Substandard / falsified drugs	Counterfeit antibiotics, fake insulin
Drug abuse & misuse	Codeine cough syrups, opioid misuse

HISTORY & DEVELOPMENT OF PHARMACOVIGILANCE

The history of pharmacovigilance is essentially a history of disasters — every major progress has come after a tragedy. Pharmacy students MUST memorize this timeline because it appears in almost every B.Pharm exam as a 5 or 10-mark question.

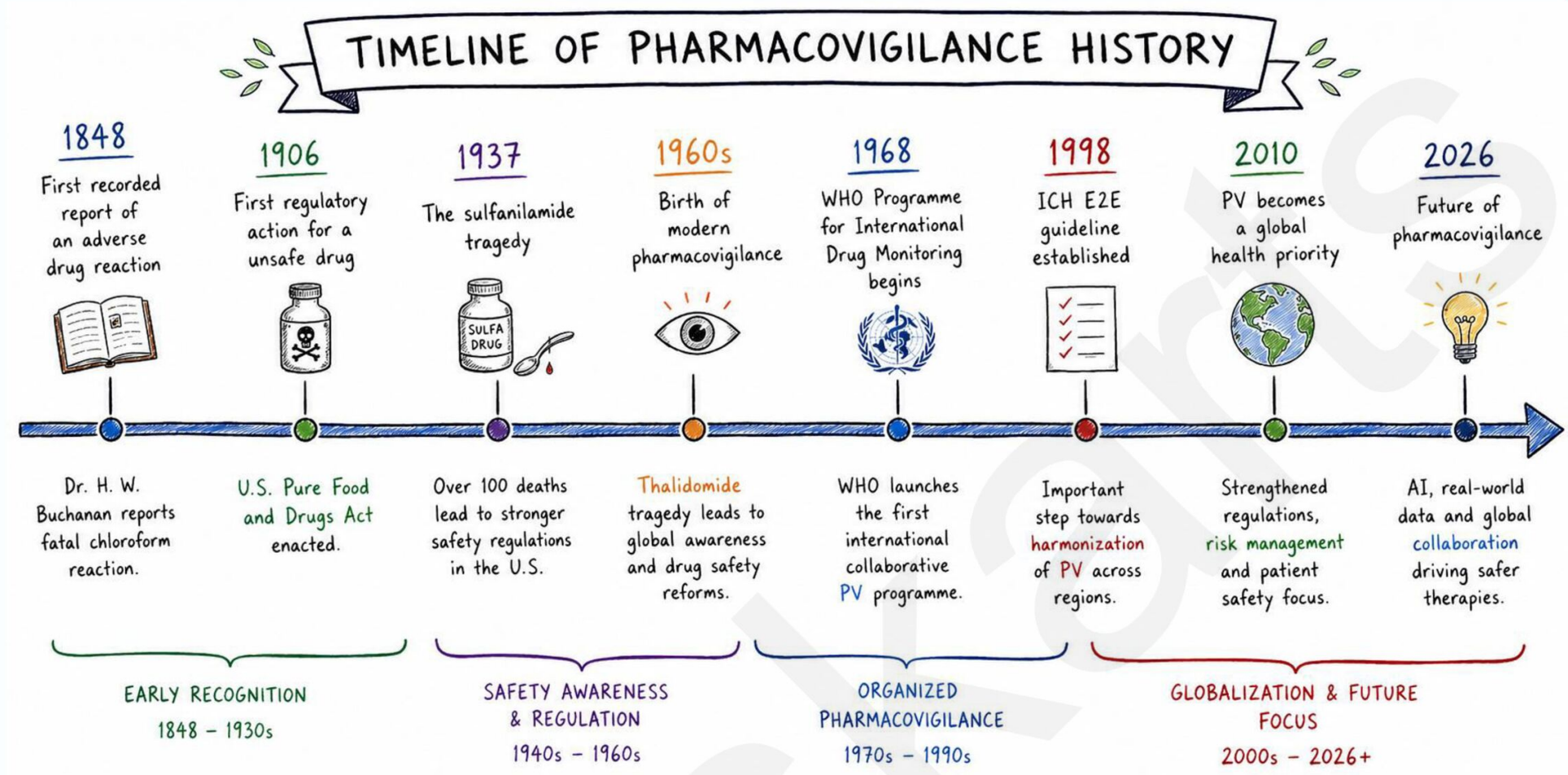
Pre-Thalidomide Era — Early Warnings

Year	Event	Outcome
1848	Hannah Greener (15-yr girl) died from chloroform anaesthesia in UK	First documented anaesthetic death
1880	Cocaine addiction reported	First addiction surveillance
1922	Jaundice with arsenicals (Salvarsan)	Need for systemic monitoring
1937	Sulfanilamide–DEG tragedy (USA) — 107 deaths (mostly children) from diethylene glycol solvent	→ US FDC Act 1938 (safety testing mandatory)
1954	Stalinon® (organotin) tragedy in France — 100+ deaths from staphylococcal infections	Need for proper drug testing

The Thalidomide Disaster (1961) — The Game Changer

⚠ THE TRAGEDY THAT BUILT PHARMACOVIGILANCE

Drug: **Thalidomide — sold as** *Contergan®, Distaval®* as a sedative/anti-emetic for morning sickness in pregnancy (1957).
Disaster: Over 10,000 babies born with ***phocomelia*** (seal-like limbs) and other limb deformities in 46 countries.
Hero: Dr. **Frances Oldham Kelsey** (FDA reviewer) blocked thalidomide in USA — saved thousands of American babies.
Whistleblower: Dr. **William McBride** (Australian obstetrician) published the link in *The Lancet* in December 1961.
Result: WHO launched the **International Drug Monitoring Programme in 1968.** This is the BIRTH of modern pharmacovigilance.



→ 1848 — Hannah Greener (chloroform death)
→ 1937 — Sulfanilamide-DEG tragedy
→ 1961 — THALIDOMIDE DISASTER (highlight in red)
→ 1963 — WHO Resolution WHA 16.36
→ 1968 — WHO Pilot Drug Monitoring Programme
→ 1978 — Uppsala Monitoring Centre (Sweden)
→ 1986 — India joins WHO Programme
→ 1997 — India officially member of WHO-UMC
→ 2010 — Pharmacovigilance Programme of India (PvPI) launched
→ 2011 — IPC, Ghaziabad becomes NCC-PvPI
→ 2017 — VigiFlow adopted in India
→ 2026 — Present day (you are here!)

Post-Thalidomide Milestones

Year	Milestone
1963	16th World Health Assembly Resolution WHA 16.36 — called for systemic drug monitoring
1968	WHO Pilot Research Project for International Drug Monitoring launched with 10 countries
1971	First ADR database in WHO
1978	Coordinating centre shifted to Uppsala, Sweden → Uppsala Monitoring Centre (UMC)
1986	India joined the WHO programme (initially withdrew)
1997	India became an official member of WHO Programme for International Drug Monitoring
1998	National Pharmacovigilance Centre established (later discontinued)
2002	WHO defined pharmacovigilance formally
2004	Vioxx (rofecoxib) withdrawn worldwide for cardiac events
2005	National Pharmacovigilance Programme by CDSCO (failed)
14 July 2010	Pharmacovigilance Programme of India (PvPI) launched by Ministry of H&FW
April 2011	IPC, Ghaziabad became National Coordinating Centre (NCC) for PvPI

Year	Milestone
2017	PvPI adopted VigiFlow as reporting software

IMPORTANCE OF SAFETY MONITORING OF MEDICINES

Bahot students yeh galti karte hain — they think "if a drug passed clinical trials, it must be safe." GALAT! Clinical trials have major limitations, and that's why post-marketing surveillance is mandatory.

Why Pre-Marketing Trials Are NOT Enough — The "5 Toos" Rule

Clinical trials are limited by what researchers call the "5 Toos":

Limitation	Explanation	Real Example
Too Few	Only 500–5000 patients in trials; rare ADRs (1 in 10,000) get missed	Vioxx — cardiac events found only after 80 million users
Too Simple	Patients with multiple diseases / multiple drugs excluded	Drug interactions appear only in real practice
Too Median-aged	Pediatric, geriatric, pregnant patients excluded	Thalidomide — never tested in pregnant women
Too Narrow	Studied for specific indication only; off-label use missed	Gabapentin — off-label psychiatric use ADRs
Too Brief	Trials usually 6 months–2 years; long-term effects unknown	Cisapride — fatal arrhythmias after years of use

Reasons for Post-Marketing Pharmacovigilance

1. Detection of rare ADRs (incidence <1 in 10,000).
2. Detection of delayed/long-latency ADRs (e.g., DES → vaginal cancer 20 yrs later).
3. Detection of ADRs in special populations (pregnant, paediatric, geriatric, hepatic/renal impaired).
4. Drug-drug, drug-food, drug-herb interactions in real-world use.
5. Medication errors (wrong dose, wrong route, look-alike sound-alike — LASA drugs).
6. Off-label use and misuse.
7. Quality issues — counterfeit/substandard drugs.
8. Promotion of rational drug use and cost-effective therapy.
9. Regulatory decision-making (label changes, withdrawals, restrictions).
10. Building public confidence in healthcare system.

IN INDIAN CONTEXT — DRUGS WITHDRAWN IN INDIA

✓ **Rofecoxib (Vioxx) —** withdrawn 2004 (cardiac events)
✓ **Cisapride —** withdrawn (QT prolongation, arrhythmia)
✓ **Phenylpropanolamine —** withdrawn (stroke risk)
✓ **Nimesulide (paediatric) —** banned in <12 yrs in India (2011) for hepatotoxicity
✓ **Analgin (Metamizole) —** banned in India (2013) for agranulocytosis
✓ **Sibutramine —** withdrawn 2010 (cardiac events)

WHO INTERNATIONAL DRUG MONITORING PROGRAMME

This is the world's biggest drug safety network. It was started in 1968 with just 10 countries, and today over 170 countries are member states. India joined officially in 1997.

Structure of the WHO Programme

The WHO Programme runs through a two-level structure:

1. World Health Organization (WHO), Geneva — policy-making body. Develops global drug safety guidelines and coordinates with member states.

2. Uppsala Monitoring Centre (UMC), Uppsala, Sweden — the operational and technical centre that maintains the global ICSR database called ***VigiBase®.***

Uppsala Monitoring Centre (UMC) — Key Facts

Feature	Detail
Established	1978 (took over from WHO Geneva)
Location	Uppsala, Sweden
Status	Independent foundation since 1997
Member states	170+ countries (as of 2026)
Main database	VigiBase® — world's largest ICSR database with >35 million case reports
Software for reporting	VigiFlow (free for member countries)
Data-mining tool	VigiLyze, VigiMatch
Dictionary used	WHODrug (drug names) + WHO-ART / MedDRA (adverse reactions)
Publications	Uppsala Reports (quarterly magazine), WHO Pharmaceuticals Newsletter
Key role	Signal detection — identifying new safety signals from global data

How the WHO Programme Works — Reporting Flow

WHO INTERNATIONAL DRUG MONITORING – DATA FLOW

5
WHO GENEVA
Global regulatory decisions

WHO GENEVA
Global regulatory decisions
- Policy & guideline development
- Signal assessment
- Regulatory actions
- Communication to countries

Aggregated safety data

Feedback, guidance, safety alerts

4
UPPSALA MONITORING CENTRE (UMC), SWEDEN
Feeds into VigiBase®

UPPSALA MONITORING CENTRE
(UMC), Sweden
- Receives ICSRs from NCCs
- Data quality check & standardization
- Causality assessment support
- Enters data into VigiBase®

UMC

VigiBase®

Aggregated safety data

Feedback, guidance, signals, alerts

3
NATIONAL COORDINATING CENTRE (NCC)
e.g., IPC Ghaziabad (India)

NATIONAL COORDINATING CENTRE
(e.g., IPC Ghaziabad for India)
- Collects ADR reports from AMCs
- Data validation & analysis
- Forwards ICSRs to UMC
- Disseminates safety information

Individual case safety reports (ICSRs)

Feedback, training, safety updates

2
ADR MONITORING CENTRE (AMC)
in Hospitals

ADR MONITORING CENTRE (AMC)
in Hospitals
- Collects ADR information
- Verifies & documents reports
- Enters data into national database
- Forwards to NCC

ADR reports

Feedback, awareness, resources

1
HEALTHCARE PROFESSIONALS / PATIENTS (REPORTERS)

HEALTHCARE PROFESSIONALS / PATIENTS (REPORTERS)
- Detect & identify ADRs
- Report suspected ADRs
- Provide patient information

→ Flow of data (reports move upward)

--→ Flow of feedback (information moves downward)

Working together for patient safety:
Collect → Assess → Understand → Act → Communicate

Functions of UMC

- Maintain global ICSR database (VigiBase®).
- Detect early signals of drug safety problems.
- Provide training, software (VigiFlow), and technical support to national centres.
- Publish standards, guidelines, and the WHO-ART / MedDRA terminologies.
- Coordinate annual meetings of representatives from member countries.
- Research and develop new pharmacovigilance methods.

PHARMACOVIGILANCE PROGRAMME OF INDIA (PvPI)

PvPI is India's flagship drug safety programme. Yeh question 100% aata hai exam mein — guaranteed.

PvPI —Facts

Parameter	Details
Launched on	14 July 2010
Launched by	Ministry of Health & Family Welfare, Government of India
Initial NCC	AIIMS, New Delhi (2010)
Current NCC (since 15 April 2011)	Indian Pharmacopoeia Commission (IPC), Ghaziabad, U.P.
Regulatory authority	CDSCO (Central Drugs Standard Control Organisation)
Current ADR Monitoring Centres (AMCs)	300+ across India (govt & private medical colleges, corporate hospitals)
Software used	VigiFlow (since 2017)
Helpline	1800-180-3024 (toll-free)
Mobile app	ADR PvPI (available on Play Store)
Reporting form	Suspected ADR Reporting Form (red form for HCPs, blue/consumer form for patients)

Vision and Mission of PvPI

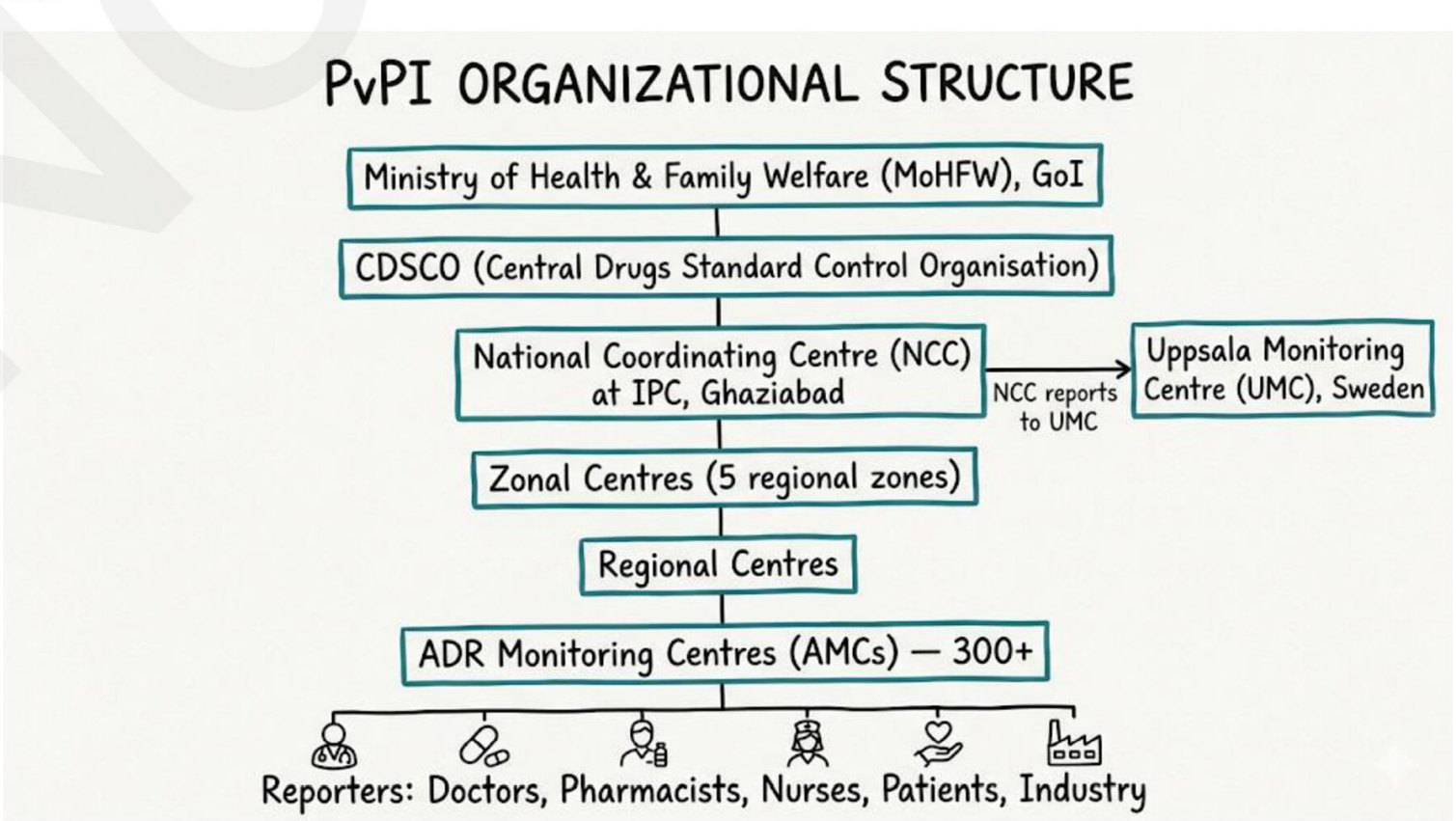
Vision: To improve patient safety and welfare in the Indian population by monitoring drug safety and thereby reducing the risk associated with use of medicines.

Mission: To safeguard the health of the Indian population by ensuring that the benefit of use of medicine outweighs the risks associated with its use.

Objectives of PvPI

1. To monitor adverse drug reactions in Indian population.
2. To create awareness amongst healthcare professionals about the importance of ADR reporting.
3. To collaborate with WHO-UMC and contribute Indian data to VigiBase®.
4. To generate independent, evidence-based recommendations on safety of medicines.
5. To support CDSCO for formulating safety-related regulatory decisions for medicines.
6. To communicate the findings to all key stakeholders.
7. To emerge as a national centre of excellence for pharmacovigilance activities.

Structure of PvPI



Stakeholders of PvPI

Stakeholder	Role
MoHFW	Policy framework, funding
CDSCO	Regulatory authority, drug approvals/withdrawals
IPC, Ghaziabad (NCC)	National coordination of ADR monitoring
AMCs (300+)	Collect ADR reports from hospitals/clinics
Healthcare Professionals	Identify and report ADRs
Pharma Industry (MAHs)	Report ADRs as PSURs, ICSRs
Consumers/Patients	Direct reporting via mobile app or form
WHO-UMC	Receives Indian data into VigiBase®

ADR Reporting in PvPI — Who Can Report?

Following persons can report ADRs to PvPI:

- Doctors, Dentists, Nurses, Pharmacists, and other healthcare professionals.
- Patients and consumers (since 2018 in PvPI).
- Marketing Authorisation Holders (MAH) i.e., pharma companies.
- Researchers/Investigators of clinical trials.

COMMON EXAM TRICK

Examiners love asking: "Where is the National Coordinating Centre (NCC) of PvPI located?"

✓ **Correct answer:** Indian Pharmacopoeia Commission (IPC), Ghaziabad, Uttar Pradesh.

✗ **Wrong (trap) answer:** AIIMS, New Delhi — this WAS the NCC only from 2010 to April 2011. Many students mark this incorrectly!

ADVERSE DRUG REACTIONS — DEFINITIONS & CLASSIFICATION

WHO Definition of ADR (1972)

WHO DEFINITION OF ADR

"Any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for modification of physiological function."

noxious + unintended + normal doses (excludes overdose). Memorize these 3 words!

Rawlins-Thompson Classification (Type A to F) — MOST IMPORTANT

This is the classical classification published by Michael Rawlins and Judith Thompson (1977). Originally had 2 types (A & B), later expanded to A–F. Hamesha exam mein aata hai.

Type	Name	Characteristics	Examples
A	Augmented (Pharmacological)	Dose-related, predictable, common (>80%), low mortality, dose-↓ helps	Bleeding with warfarin; hypoglycemia with insulin; bradycardia with β-blockers
B	Bizarre (Hypersensitivity / Idiosyncratic)	Not dose-related, unpredictable, rare, high mortality, must STOP drug	Penicillin anaphylaxis; SJS with carbamazepine; halothane hepatitis
C	Chronic (Continuous use)	Dose & time-related, predictable, due to long-term use	Steroid-induced osteoporosis/Cushing's; analgesic nephropathy
D	Delayed	Time-related, appears years later, often after stopping drug	Tardive dyskinesia (antipsychotics); carcinogenesis; teratogenesis (thalidomide)
E	End-of-use (Withdrawal)	Occurs on sudden discontinuation	Beta-blocker rebound HTN; opioid withdrawal; benzodiazepine withdrawal seizures

Type	Name	Characteristics	Examples
F	Failure of therapy	Unexpected therapeutic failure, often interactions	OC pill failure with rifampicin/phenytoin (enzyme induction)

Type A vs Type B — The Most-Asked Comparison

Feature	Type A (Augmented)	Type B (Bizarre)
Frequency	Common (~80% of ADRs)	Rare (~10–15%)
Dose-related?	YES	NO
Predictability	Predictable	Unpredictable
Mortality	Low	High
Mechanism	Exaggerated pharmacology	Immune/idiosyncratic
Management	Reduce dose	Stop drug immediately
Detection	Pre-marketing trials	Post-marketing surveillance
Example	Bleeding with warfarin	Anaphylaxis with penicillin

Wills & Brown Classification (2009)

This classification extends Rawlins-Thompson to 9 types:

Type	Description
Type A — Augmented	Pharmacological, dose-related
Type B — Bugs	Drug favours infection (e.g., antibiotic → C. difficile colitis)
Type C — Chemical	Chemical irritation (e.g., extravasation with chemotherapy)
Type D — Delivery	ADR from drug delivery system (e.g., IUD perforation)
Type E — Exit	Withdrawal reactions
Type F — Familial	Genetic predisposition (e.g., G6PD deficiency with primaquine)
Type G — Genotoxic	DNA damage (carcinogens like thalidomide, DES)
Type H — Hypersensitivity	Immune reactions
Type U — Unclassified	Mechanism unknown (e.g., nausea with most drugs)

DoTS Classification (Aronson & Ferner, 2003)

DoTS = Dose, Time, Susceptibility. A modern way to classify ADRs based on 3 dimensions:

- **Do** → Dose-relationship: *Toxic* (above therapeutic), *Collateral* (at therapeutic), *Hypersusceptibility* (below therapeutic)
- **T** → Time-course: *Time-independent* vs *Time-dependent* (rapid, first-dose, early, intermediate, late, delayed)
- **S** → Susceptibility factors: age, sex, disease, genetic, exogenous factors (other drugs, food)

Other Important Classifications

Classification	Basis
Severity-based (Hartwig)	Mild / Moderate / Severe
Mechanism-based	Pharmacological / Idiosyncratic / Allergic / Pseudo-allergic
Pharmacological	Type 1 (IgE), Type 2 (cytotoxic), Type 3 (immune complex), Type 4 (delayed) — Gell & Coombs
Body system affected	Cardiovascular, CNS, GI, dermatological, hepatic, renal, hematologic

DETECTION & REPORTING OF ADRs

Methods of ADR Detection (Pharmacovigilance Methods)

Method	Description	Advantages	Limitations
Spontaneous reporting (Yellow Card / Red Form)	Voluntary reporting by HCPs/patients	Cheap, easy, covers all drugs	Under-reporting (~5–10%), no denominator
Cohort event monitoring (CEM)	Follow-up of patients on a particular drug	Captures all events, good for new drugs	Expensive, time-consuming
Case-control study	Compares patients with ADR vs without	Good for rare ADRs	Recall bias
Prescription event monitoring (PEM)	PEM cards sent to prescribers	Real-world data	Low response rate
Record linkage	Computer-linked databases (claims, EHR)	Large population	Data quality issues
Meta-analysis	Pooled analysis of multiple studies	High statistical power	Heterogeneity
Targeted clinical investigations	Specifically designed for a safety question	High quality data	Expensive

Spontaneous Reporting in India

Spontaneous reporting is the BACKBONE of pharmacovigilance in India. Reports are made on the Suspected ADR Reporting Form (CDSCO/PvPI form).

The form has 4 essential elements (mnemonic = "PRDR" — Patient, Reaction, Drug, Reporter):

Element	Information Required
1. Patient	Initials, age, sex, weight, relevant medical history
2. Reaction (ADR)	Description, date of onset, duration, outcome, seriousness
3. Suspected drug(s)	Name, dose, route, frequency, indication, start/stop dates, batch number
4. Reporter	Name, designation, address, contact, signature, date

INDIAN ADR FORM TYPES

Red Form (HCP form): For doctors, pharmacists, nurses — detailed 4-page form.
Blue Form (Consumer form): For patients/caregivers — simpler version. Launched 2018.
Available at: www.ipc.gov.in or ADR PvPI mobile app.

Reasons for Under-Reporting (Inman's "Deadly Sins")

Dr W. Inman described 7 deadly sins that prevent doctors from reporting ADRs:

1. Complacency — "only safe drugs are marketed"
2. Fear — of litigation/medical liability
3. Guilt — caused harm to patient
4. Ambition — to publish a series of cases later
5. Ignorance — about how/where to report
6. Diffidence/Shyness — fear of reporting something silly
7. Lethargy — too busy, no time

MNEMONIC — "C-FAGILD"

Complacency, **F**ear, **A**mbition, **G**uilt, **I**gnorance, **L**ethargy, **D**iffidence.

METHODS OF CAUSALITY ASSESSMENT

Causality assessment is the process of determining the likelihood that a drug caused a particular ADR. Multiple scales exist — but for B.Pharm exams, the top 2 are WHO-UMC and Naranjo.

WHO-UMC Causality Categories (6 Levels)

Category	Description
Certain	Plausible time relationship; cannot be explained by other drugs/disease; clear response to withdrawal (dechallenge) and rechallenge positive
Probable / Likely	Reasonable time relationship; unlikely due to other drug/disease; reasonable response to withdrawal; rechallenge not required
Possible	Reasonable time relationship; could be explained by other drugs/disease; information on withdrawal lacking or unclear
Unlikely	Improbable time relationship; other drugs/disease provide plausible explanation
Conditional / Unclassified	More data needed for proper assessment
Unassessable / Unclassifiable	Report suggests ADR but cannot be judged due to insufficient/contradictory information

Naranjo Algorithm / Scale (1981) — Most Important for Exams

Developed by Claudio Naranjo. Has 10 questions, each scored +1, 0, or -1. Total score interprets causality.

#	Question	Yes	No	Don't Know
1	Are there previous conclusive reports on this reaction?	+1	0	0
2	Did the ADR appear after the suspected drug was administered?	+2	-1	0
3	Did the ADR improve when the drug was discontinued or a specific antagonist administered?	+1	0	0
4	Did the ADR reappear when drug was readministered (rechallenge)?	+2	-1	0
5	Are there alternative causes (other than the drug) that could have caused the reaction?	-1	+2	0
6	Did the reaction reappear when placebo was given?	-1	+1	0
7	Was the drug detected in blood/body fluids in toxic concentration?	+1	0	0
8	Was the reaction more severe when dose was increased / less severe when decreased?	+1	0	0
9	Did the patient have similar reaction to the same or similar drug in any previous exposure?	+1	0	0
10	Was the ADR confirmed by any objective evidence?	+1	0	0

Naranjo Score Interpretation:

Total Score	Causality Category
≥ 9	Definite ADR
5 – 8	Probable ADR
1 – 4	Possible ADR
≤ 0	Doubtful ADR

Other Causality Assessment Scales

Scale	Year	Author / Use
WHO-UMC scale	—	Qualitative; used by WHO and PvPI
Naranjo Algorithm	1981	Most widely used; 10-question scoring
Karch-Lasagna	1977	Earliest scale; 5 categories

Scale	Year	Author / Use
Kramer's algorithm	1979	Most detailed but complex
Begaud / French method	1985	Used in France; semi-quantitative
Roussel-Uclaf Causality Assessment Method (RUCAM)	1993	Specifically for drug-induced liver injury (DILI)

SEVERITY, SERIOUSNESS, PREDICTABILITY & PREVENTABILITY ASSESSMENT

Severity Assessment — Hartwig & Siegel Scale (1992)

Severity tells us HOW BAD the ADR is. Hartwig classifies it as 7 levels in 3 categories:

Category	Level	Description
MILD	1	ADR requires no change in treatment with the suspected drug
MILD	2	ADR requires that the drug be held, discontinued, or changed; no antidote or other treatment needed
MODERATE	3	ADR requires drug be held, plus specific treatment / antidote OR ↑ length of hospital stay by ≥1 day
MODERATE	4	Any level-3 ADR PLUS transfer to ICU
SEVERE	5	Any level-4 ADR causing PERMANENT harm to patient
SEVERE	6	Any level-5 ADR causing direct or indirect death of patient
SEVERE	7	Fatal ADR

Seriousness Assessment — ICH/FDA Criteria

Don't confuse SEVERITY with SERIOUSNESS — they are DIFFERENT! This is a very common exam trap.

⚡ SEVERITY vs SERIOUSNESS — KEY DIFFERENCE

Severity = intensity (mild/moderate/severe) — clinical judgement.
Seriousness = regulatory consequence (life-threatening or not) — defined by ICH-E2A criteria.
Example: A mild skin rash (severity = mild) may NOT be serious. But anaphylaxis (severity = severe) IS serious because it's life-threatening.

As per ICH-E2A, an ADR is SERIOUS if it results in any of the following (mnemonic = "DLHDIM"):

#	Criterion	Example
1	Death	Anaphylactic death
2	Life-threatening event	Massive GI bleed
3	Hospitalization (initial or prolonged)	Steven-Johnson syndrome requiring admission
4	Persistent / significant Disability / incapacity	Permanent deafness with aminoglycosides
5	Congenital anomaly / birth defect	Thalidomide → phocomelia
6	Important Medical event (requires intervention)	Bronchospasm requiring nebulization

Predictability Assessment

Predictability = whether the ADR could have been anticipated based on the drug's known pharmacology.

Type	Description	Example
Predictable	Dose-related, known pharmacology — Type A ADR	Drowsiness with antihistamines; constipation with opioids
Unpredictable	Not dose-related, idiosyncratic — Type B ADR	Penicillin anaphylaxis; SJS with carbamazepine

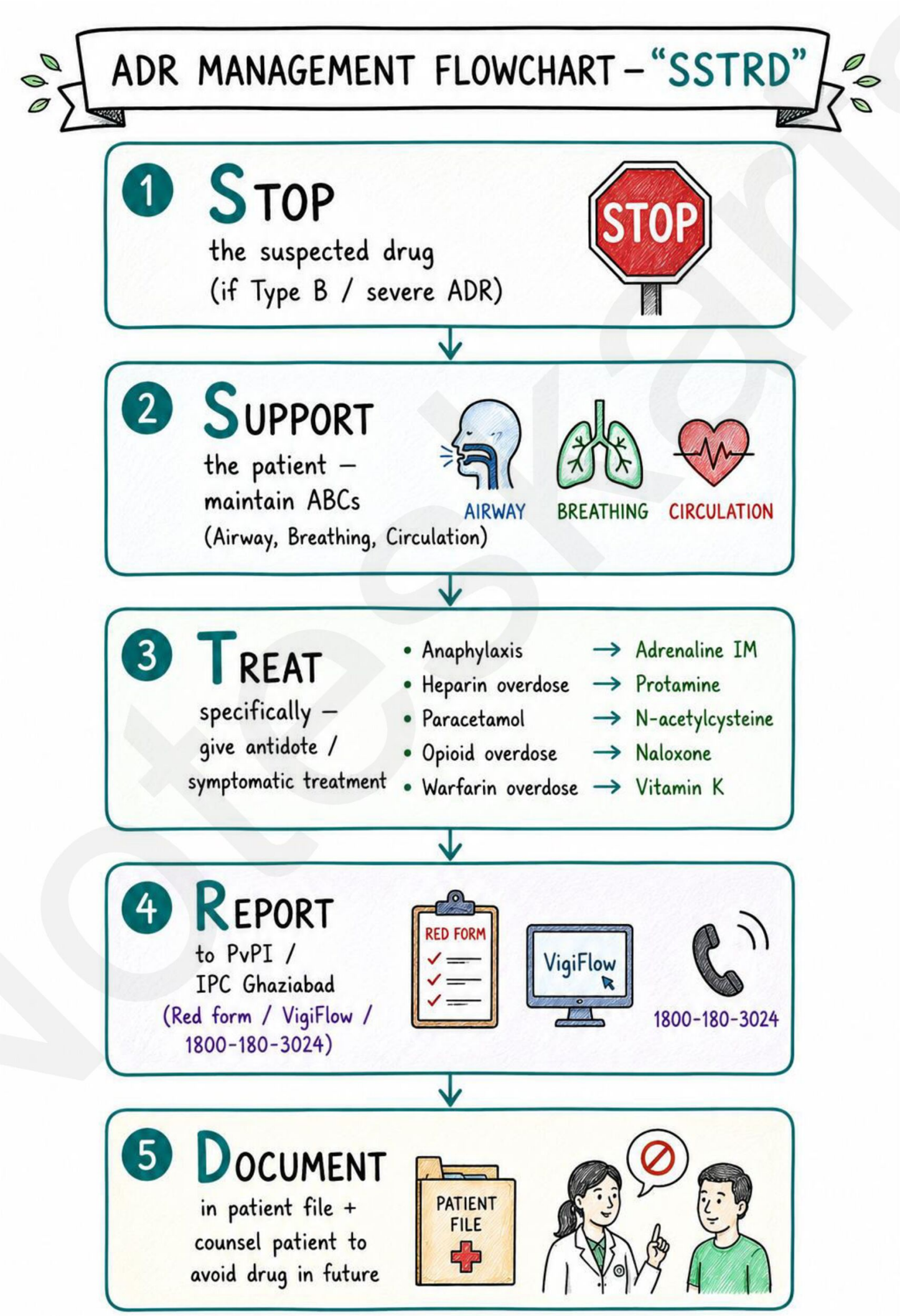
Preventability Assessment — Schumock & Thornton Criteria (1992)

Preventability = whether the ADR could have been avoided by appropriate action. Schumock-Thornton classifies ADRs into 3 categories using a series of questions:

Category	Criteria (any "YES" places ADR in this category)
Definitely Preventable	Drug not appropriate for clinical condition / dose, route, frequency inappropriate for patient / required therapeutic drug monitoring not performed / history of allergy known but drug given / drug interaction involved / toxic serum drug level documented / poor compliance noted
Probably Preventable	Drug dose adjustment not made for impaired renal/hepatic function / appropriate preventive measure not administered / non-compliance contributed but not solely
Not Preventable	ADR could not have been prevented by any reasonable means — typically Type B reactions (e.g., unforeseen anaphylaxis)

ADR Management — General Approach

When an ADR occurs, follow the SSTRD approach:



PHARMACOVIGILANCE TERMINOLOGIES

This section is a MCQ goldmine. Examiners love testing the subtle differences between AE, ADE, ADR, SAE, etc. Master these definitions verbatim.

Terminologies of Adverse Medication-Related Events

Term	Abbreviation	Definition
Adverse Event	AE	Any untoward medical occurrence in a patient on a medicinal product, which does NOT necessarily have causal relationship with treatment
Adverse Drug Event	ADE	Any injury resulting from the use of a drug — includes both ADRs and medication errors
Adverse Drug Reaction	ADR	A noxious and unintended response to a drug at normal therapeutic doses — causal relationship established
Side Effect	SE	Any unintended effect of a drug at therapeutic dose — may be beneficial OR harmful
Serious Adverse Event	SAE	Any AE resulting in death, life-threatening event, hospitalization, persistent disability, congenital anomaly, or important medical event
Unexpected ADR	—	An ADR whose nature/severity is NOT consistent with the product information / package insert
Suspected Unexpected Serious Adverse Reaction	SUSAR	An ADR that is serious AND unexpected — must be reported within 7/15 days
Adverse Event Following Immunization	AEFI	Any medical event after vaccination, may or may not be caused by vaccine
Signal	—	Reported information on a possible causal relationship between an AE and a drug, previously unknown or incompletely documented
Medication Error	ME	Any preventable event causing inappropriate medication use or patient harm (wrong drug, wrong dose, wrong route, wrong patient, wrong time)
Side Effect vs Toxic Effect	—	Side effect = at therapeutic dose; Toxic effect = at overdose

Regulatory Terminologies

Term	Abbreviation	Definition
Individual Case Safety Report	ICSR	Report describing AE in one patient at one point in time (basic unit of PV reporting)
Periodic Safety Update Report	PSUR	Periodic safety report submitted by MAH to regulators (every 6 months for new drugs, then annually)
Periodic Adverse Drug Experience Report	PADER	US-FDA's equivalent of PSUR; quarterly for first 3 years
Periodic Benefit-Risk Evaluation Report	PBRER	Replaced PSUR in EU (ICH-E2C R2 format)
Development Safety Update Report	DSUR	Annual safety report during clinical development (ICH-E2F)
Marketing Authorisation Holder	MAH	Pharma company licensed to market a drug; responsible for PV
Risk Management Plan	RMP	Document describing risk minimization activities for a drug
Direct Healthcare Professional Communication	DHPC	Letter sent by MAH/regulator to HCPs about new safety information
Council for International Organizations of Medical Sciences	CIOMS	Develops PV guidelines; CIOMS-I = ICSR form
International Conference on Harmonisation	ICH	Harmonizes drug regulation; E2A-E2F = PV guidelines
Good Pharmacovigilance Practices	GVP	EMA guidelines for PV (16 modules)
MedDRA	—	Medical Dictionary for Regulatory Activities — standard terminology for AE coding
WHODrug	—	WHO global drug dictionary
VigiBase®	—	WHO global ICSR database at UMC
VigiFlow	—	Web-based ICSR management system by UMC

Time-Related Terms

Term	Definition
Dechallenge	Withdrawal of the suspected drug to see if ADR resolves; positive dechallenge = ADR resolves
Rechallenge	Re-administration of the suspected drug to confirm ADR; positive rechallenge = ADR recurs (strongest evidence)
Day Zero	Date of receipt of valid ICSR by MAH or regulator — clock starts here for reporting deadlines
Reporting timelines	Fatal/Life-threatening SUSAR = 7 days; Other SUSARs = 15 days; Non-serious = 90 days (in PvPI)

IMPORTANT QUESTION BANK

PART A — 2-MARK QUESTIONS (8 Qs with Model Answers)

Q1. Define pharmacovigilance.

Ans: Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems (WHO, 2002).

Q2. Name any two drugs withdrawn from the market due to ADRs.

Ans: (i) Thalidomide — withdrawn (1961) for phocomelia. (ii) Rofecoxib (Vioxx) — withdrawn (2004) for cardiac events.

Q3. What is the difference between ADR and ADE?

Ans: ADR (Adverse Drug Reaction) requires established causal relationship with the drug at therapeutic dose. ADE (Adverse Drug Event) is any harm from drug use — includes ADRs PLUS medication errors. So all ADRs are ADEs, but not all ADEs are ADRs.

Q4. When and by whom was PvPI launched?

Ans: PvPI was launched on 14 July 2010 by the Ministry of Health & Family Welfare, Government of India. The current National Coordinating Centre is IPC, Ghaziabad.

Q5. What is a Signal in pharmacovigilance?

Ans: A signal is reported information on a possible causal relationship between an adverse event and a drug, the relationship being previously unknown or incompletely documented. Usually requires more than one report to generate a signal.

Q6. Define seriousness as per ICH guidelines.

Ans: An adverse reaction is considered serious if it results in any of the following: Death, Life-threatening event, Hospitalization (initial or prolonged), persistent/significant Disability, Congenital anomaly, or any other Important medical event (mnemonic: DLHDIM).

Q7. What is the Naranjo algorithm? Mention its interpretation.

Ans: Naranjo algorithm is a 10-question causality assessment tool published in 1981. Each question scored +2/+1/0/–1. Total score interpretation: ≥9 = Definite ADR, 5–8 = Probable, 1–4 = Possible, ≤0 = Doubtful.

Q8. Expand the following: WHO, UMC, ICSR, PSUR.

Ans: WHO = World Health Organization; UMC = Uppsala Monitoring Centre; ICSR = Individual Case Safety Report; PSUR = Periodic Safety Update Report.

PART B — 5-MARK QUESTIONS (5 Qs with Model Answer Outlines)

- **Q1. Explain the Rawlins-Thompson classification of ADRs with examples.**
- **Q2. Write a note on the Thalidomide tragedy and its impact on pharmacovigilance.**
- **Q3. Describe the structure and functions of PvPI.**
- **Q4. Explain the Naranjo algorithm for causality assessment.**
- **Q5. Differentiate between Type A and Type B adverse drug reactions.**

PART C — 10-MARK QUESTIONS (3 Qs with Complete Outlines)

- **Q1. Define pharmacovigilance. Discuss its history, importance of safety monitoring of medicines, and the WHO international drug monitoring programme.**
- **Q2. Classify Adverse Drug Reactions in detail. Explain the methods of causality assessment with special emphasis on the Naranjo algorithm.**
- **Q3. Define and differentiate severity, seriousness, predictability and preventability of ADRs. Explain management of ADRs in detail.**

PREVIOUS-YEAR-STYLE QUESTIONS (5 Likely Qs)

Based on the pattern of question papers from various universities (AKTU, RGUHS, JNTU, MAKAUT, BPUT), these questions are MOST LIKELY to appear:

PYQ-1 (10 marks)

Define pharmacovigilance. Explain the history and development of pharmacovigilance with special emphasis on the Pharmacovigilance Programme of India (PvPI).

PYQ-2 (10 marks)

What is an Adverse Drug Reaction? Classify ADRs in detail. Add a note on causality and severity assessment of ADRs.

PYQ-3 (5 marks)
Write short note on: (a) Type A vs Type B ADR (b) Naranjo Algorithm

PYQ-4 (5 marks)
Define and explain the following pharmacovigilance terminologies: ADR, AE, ADE, SAE, AEFI.

PYQ-5 (2 marks)
What are the seriousness criteria for ADRs as per ICH-E2A?

✓ TOP 25 EASY MCQs (with Detailed Explanations)

These 25 EASY MCQs cover recall and definition-based questions. Master these and you'll easily score 8-10/10 in any MCQ section of pharmacovigilance.

Q1. Pharmacovigilance is defined by which organization?

A) FDA
B) WHO
C) CDSCO
D) ICMR

Answer: B — *WHO defined pharmacovigilance in 2002 as the science of detection, assessment, understanding and prevention of adverse effects.*

Q2. The term 'Pharmacovigilance' is derived from which two roots?

A) Pharmakon + Vigilare
B) Pharma + Vision
C) Pharmacy + Vigil
D) Pharmakos + Vigil

Answer: A — *From Greek 'Pharmakon' (drug) + Latin 'Vigilare' (to keep watch). Literally means 'keeping watch on drugs'.*

Q3. The Thalidomide tragedy occurred in which year?

A) 1956
B) 1961
C) 1968
D) 1972

Answer: B — *Thalidomide-induced phocomelia was reported by Dr McBride in The Lancet in December 1961. This led to the WHO drug monitoring programme in 1968.*

Q4. WHO International Drug Monitoring Programme was started in which year?

A) 1961
B) 1968
C) 1978
D) 1997

Answer: B — *The WHO Pilot Research Project for International Drug Monitoring was launched in 1968 with 10 founding member countries.*

Q5. The Uppsala Monitoring Centre (UMC) is located in which country?

A) Switzerland
B) Norway
C) Sweden
D) Denmark

Answer: C — *UMC is in Uppsala, Sweden. It became the operational centre of WHO Programme in 1978.*

Q6. Pharmacovigilance Programme of India (PvPI) was launched on:

A) 14 July 2010
B) 15 August 2010
C) 14 April 2011
D) 1 January 2012

Answer: A — *PvPI was officially launched on 14 July 2010 by the Ministry of Health & Family Welfare, GoI.*

Q7. The current National Coordinating Centre (NCC) of PvPI is located at:

A) AIIMS, New Delhi
B) IPC, Ghaziabad
C) NIPER, Mohali
D) CDRI, Lucknow

Answer: B — *Since 15 April 2011, IPC (Indian Pharmacopoeia Commission) Ghaziabad has been the NCC for PvPI. AIIMS Delhi was NCC only from 2010 to April 2011 — a common exam trap!*

Q8. Penicillin-induced anaphylaxis is an example of which type of ADR?

A) Type A
B) Type B

C) Type C
D) Type D

Answer: B — *Penicillin anaphylaxis is unpredictable, not dose-related, idiosyncratic/hypersensitivity → Type B (Bizarre) ADR.*

Q9. Bleeding due to warfarin is an example of which type of ADR?

A) Type A
B) Type B
C) Type C
D) Type E

Answer: A — *Warfarin bleeding is dose-related, predictable, due to its anticoagulant pharmacology → Type A (Augmented) ADR.*

Q10. Steroid-induced osteoporosis is an example of which type of ADR?

A) Type A
B) Type B
C) Type C
D) Type D

Answer: C — *Steroid osteoporosis appears after long-term continuous use → Type C (Chronic) ADR.*

Q11. Tardive dyskinesia caused by antipsychotics is which type of ADR?

A) Type B
B) Type C
C) Type D
D) Type F

Answer: C — *Tardive dyskinesia appears years after starting antipsychotics → Type D (Delayed) ADR.*

Q12. Naranjo algorithm has how many questions?

A) 8
B) 10
C) 12
D) 15

Answer: B — *The Naranjo algorithm (1981) consists of 10 questions, each scored +2, +1, 0, or -1.*

Q13. A Naranjo score of 9 indicates which causality?

A) Possible
B) Probable
C) Definite
D) Doubtful

Answer: C — *Score ≥9 = Definite. Score 5-8 = Probable. Score 1-4 = Possible. Score ≤0 = Doubtful.*

Q14. The Hartwig scale is used to assess:

A) Causality
B) Severity
C) Preventability
D) Predictability

Answer: B — *Hartwig & Siegel scale (1992) assesses severity of ADR in 7 levels — mild (1-2), moderate (3-4), severe (5-7).*

Q15. Schumock-Thornton criteria is used to assess:

A) Severity
B) Predictability
C) Preventability
D) Causality

Answer: C — *Schumock & Thornton (1992) assesses preventability of ADRs — Definitely preventable, Probably preventable, Not preventable.*

Q16. ICSR stands for:

A) International Case Safety Report
B) Individual Case Safety Report
C) Indian Case Surveillance Report
D) Industrial Case Safety Report

Answer: B — *ICSR = Individual Case Safety Report — the basic unit of pharmacovigilance reporting describing one patient at one time point.*

Q17. PSUR stands for:

A) Patient Safety Update Report
B) Periodic Safety Update Report
C) Pharmacovigilance Safety Update Report
D) Post-marketing Safety Update Report

Answer: B — *PSUR = Periodic Safety Update Report submitted by MAH to regulators every 6 months initially, then annually.*

Q18. Which is NOT a seriousness criterion as per ICH-E2A?

A) Death
B) Hospitalization
C) Skin rash
D) Congenital anomaly

Answer: C — *Mild skin rash is NOT a seriousness criterion. The 6 criteria are: Death, Life-threatening, Hospitalization, Disability, Congenital anomaly, Important medical event (DLHDIM).*

Q19. AEFI stands for:

A) Adverse Effects from Injection
B) Adverse Event Following Immunization
C) Acute Effect of Injection
D) Adverse Effect of Infusion

Answer: B — *AEFI = Adverse Event Following Immunization — any medical event after vaccination (may or may not be caused by the vaccine).*

Q20. The global ADR database maintained by UMC is called:

A) VigiFlow
B) VigiBase®
C) VigiLyze
D) MedWatch

Answer: B — *VigiBase® is the WHO global database of ICSRs at Uppsala Monitoring Centre — contains 35+ million reports as of 2026.*

Q21. MedDRA stands for:

A) Medical Drug Reactions Atlas
B) Medical Dictionary for Regulatory Activities
C) Medication Database for Reporting Adverse events
D) Medicine Directory of Reactions

Answer: B — *MedDRA = Medical Dictionary for Regulatory Activities — the standard terminology for coding adverse events in pharmacovigilance worldwide.*

Q22. Withdrawal of a drug to see if ADR resolves is called:

A) Rechallenge
B) Dechallenge
C) Crosschallenge
D) Preempt challenge

Answer: B — *Dechallenge = stopping the suspected drug to observe if ADR improves. Positive dechallenge = ADR resolves. Rechallenge is restarting the drug.*

Q23. India officially joined the WHO Programme for International Drug Monitoring in:

A) 1986
B) 1997
C) 2005
D) 2010

Answer: B — *India became a member in 1986, withdrew, and rejoined officially in 1997. PvPI was launched much later in 2010.*

Q24. Phocomelia is the characteristic teratogenic effect of which drug?

A) Cisapride
B) Thalidomide
C) Rofecoxib
D) Sibutramine

Answer: B — *Thalidomide causes phocomelia (seal-like limb deformity) — the tragedy that led to the creation of modern pharmacovigilance in the 1960s.*

Q25. Which type of ADR is best detected by post-marketing surveillance?

A) Type A
B) Type B
C) Both A and B
D) Neither

Answer: B — *Type B (bizarre/idiosyncratic) ADRs are rare and unpredictable, so they are often missed in pre-marketing trials and are best detected by post-marketing surveillance.*