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PREMIUM STUDY NOTES

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B.PHARM 8th SEMESTER BP805ET — PHARMACOVIGILANCE UNIT — II

*Drug & Disease Classification • Drug Dictionaries • Information Resources •
Establishing PV Programmes*

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

ANATOMICAL, THERAPEUTIC & CHEMICAL CLASSIFICATION OF DRUGS

Introduction to ATC Classification

The Anatomical Therapeutic Chemical (ATC) classification system is the international standard maintained by the WHO Collaborating Centre for Drug Statistics Methodology, Oslo, Norway. It classifies drugs at 5 hierarchical levels based on the organ/system they act on, their therapeutic and pharmacological properties, and their chemical properties.

DEFINITION

ATC Classification System: A system in which drugs are classified into groups at five different levels according to the organ or system on which they act, and their therapeutic, pharmacological, and chemical properties (WHO, Oslo).

The Five Levels of ATC Classification

Each drug gets a unique ATC code. Let's understand using the classic example: Metformin (anti-diabetic drug).

Level	Name	Description	Metformin Example	No. of Groups
1st	Anatomical Main Group	Organ/system affected	A (Alimentary tract & metabolism)	14 main groups
2nd	Therapeutic Main Group	Therapeutic use	A10 (Drugs used in Diabetes)	~96 groups
3rd	Therapeutic/Pharmacological Subgroup	Pharmacological class	A10B (Blood glucose lowering drugs, excl. insulins)	~250 groups
4th	Chemical/Pharmacological Subgroup	Mechanism/Chemistry	A10BA (Biguanides)	~450 groups
5th	Chemical Substance	Active ingredient	A10BA02 (Metformin)	~6,500 substances

MNEMONIC — MEMORIZE ATC CODE: "ATPCS" (Anatomy → Therapy → Pharmacology → Chemistry → Substance)

A10BA02 = A (Alimentary) → 10 (Diabetes drugs) → B (Excl. insulins) → A (Biguanides) → 02 (Metformin)

Tip: The ATC code is ALWAYS alpha-numeric: letter-number-letter-letter-number (e.g., A10BA02)

ATC Level-1 Main Groups (All 14 — Must Memorize)

Code	Anatomical Main Group	Example Drug
A	Alimentary tract and metabolism	Metformin (A10BA02), Omeprazole (A02BC01)
B	Blood and blood-forming organs	Heparin (B01AB01), Warfarin (B01AA03)
C	Cardiovascular system	Atenolol (C07AB03), Amlodipine (C08CA01)
D	Dermatologicals	Clotrimazole (D01AC01), Hydrocortisone (D07AA02)
G	Genito-urinary system and sex hormones	Sildenafil (G04BE03), OCP (G03AA07)
H	Systemic hormonal preparations, excl. sex hormones	Insulin (H01AB01), Thyroxine (H03AA01)
J	Anti-infectives for systemic use	Amoxicillin (J01CA04), Ciprofloxacin (J01MA02)
L	Antineoplastic and immunomodulating agents	Methotrexate (L01BA01), Cyclophosphamide (L01AA01)
M	Musculo-skeletal system	Ibuprofen (M01AE01), Diclofenac (M01AB05)
N	Nervous system	Aspirin (N02BA01), Paracetamol (N02BE01), Diazepam (N05BA01)
P	Antiparasitic products, insecticides, repellents	Chloroquine (P01BA01), Albendazole (P02CA03)
R	Respiratory system	Salbutamol (R03AC02), Beclomethasone (R03BA01)
S	Sensory organs	Timolol (S01ED01) for glaucoma
V	Various	Contrast media, radiopharmaceuticals

COMMON EXAM TRICK

Trick Q: Which ATC group does Paracetamol belong to? Many students answer 'A' (alimentary) thinking it's a GI drug. **WRONG!**

✓ Correct: Paracetamol = N02BE01 → Group N (Nervous system / Analgesics). Aspirin for pain = also N. Aspirin as antiplatelet = B01AC06. The SAME drug can have DIFFERENT ATC codes depending on indication!

Therapeutic Classification of Drugs

Beyond ATC, drugs are classified therapeutically based on their primary use. Key systems include:

Classification System	Basis	Example
WHO Essential Medicines List (EML)	Essential/non-essential	Amoxicillin in Core EML

Classification System	Basis	Example
BNF (British National Formulary)	Therapeutic categories	Cardiovascular, CNS sections
MIMS (Monthly Index of Medical Specialties)	Therapeutic class, India	Widely used in Indian clinical practice
DRUGDEX (Micromedex)	Evidence-based drug info	Hospital formulary decisions
Pharmacological classification	Mechanism of action	Beta-blockers, ACE inhibitors
Chemical classification	Chemical structure	Sulfonamides, fluoroquinolones

INTERNATIONAL CLASSIFICATION OF DISEASES (ICD) & DEFINED DAILY DOSES (DDD)

International Classification of Diseases (ICD)

DEFINITION

ICD: The International Classification of Diseases (ICD) is the global standard diagnostic classification maintained by WHO for medical records, health statistics, mortality, morbidity, reimbursement, and pharmacovigilance. Currently, **ICD-11** is the latest version (effective January 2022).

Structure of ICD Codes

ICD-10 (still widely used) uses alpha-numeric codes:

Code Structure	Meaning	Example
1st character (letter)	Chapter / Body System	J = Diseases of respiratory system
2nd-3rd (numbers)	Disease category	J18 = Pneumonia
4th character (after decimal)	Specific type	J18.0 = Bronchopneumonia
5th character (optional)	Further specificity	J18.00 = specific organism

ICD Version	Year	Key Feature
ICD-6	1948	First WHO version; 3-character codes
ICD-9	1977	Used for billing/claims in USA till 2015
ICD-10	1992	Alpha-numeric, 3–5 characters; still standard in many countries

ICD Version	Year	Key Feature
ICD-11	2019 (effective Jan 2022)	Digital-first, 6-character codes, better PV integration, covers traditional medicine

Relevance of ICD in Pharmacovigilance

1. Coding the indication for which a drug was prescribed.
2. Coding the ADR / medical event on the ICSR.
3. Epidemiological studies on drug-disease patterns.
4. Signal detection — linking specific disease codes with drug codes.
5. Regulatory submissions (PSUR, PBRER).
6. Denominator data for incidence calculation of ADRs.

Daily Defined Dose (DDD)

📖 DEFINITION (WHO)

Defined Daily Dose (DDD): The assumed average maintenance dose per day for a drug used for its main indication in adults (≥ 70 kg body weight). DDD is a **technical unit of measurement** and does not necessarily reflect the prescribed or recommended dose.

Feature	Details
DDD Full Form	Defined Daily Dose
Maintained by	WHO Collaborating Centre for Drug Statistics Methodology, Oslo
Purpose	Drug utilization studies, comparison across countries/time periods
Unit of expression	DDD per 1000 inhabitants per day (DID)
Linked to	ATC code — each ATC 5th-level code has one assigned DDD
Example — Metformin	DDD = 2 g oral (tablet 500 mg taken QID = 2 g/day)
Example — Aspirin (analgesic)	DDD = 3 g (N02BA01)
Example — Aspirin (antiplatelet)	DDD = 0.1 g (B01AC06)
NOT suitable for	Paediatric doses, topical drugs, vaccines, contrast media

⚡ EXAM TIP — DDD \neq Recommended Dose

DDD is NOT the prescribed dose — it is a fixed technical unit for drug utilization COMPARISON only. The SAME drug may have DIFFERENT DDDs for different ATC codes (like Aspirin). This is a very common MCQ trap!

Prescribed Daily Dose (PDD) vs DDD

Feature	DDD	PDD (Prescribed Daily Dose)
Definition	WHO technical unit for drug utilization	Actual dose prescribed by physician
Source	WHO Oslo Centre	Prescription data / patient records
Purpose	Drug utilization studies, comparative analysis	Clinical practice, pharmacoepidemiology
Fixed or variable?	Fixed (WHO-assigned)	Variable (patient-specific)
Example	Metformin DDD = 2 g	Metformin PDD may be 500 mg to 3 g
Who uses it	Drug utilization researchers, regulators	Clinicians, hospital pharmacists

INTERNATIONAL NON-PROPRIETARY NAMES (INN) FOR DRUGS

Definition and Purpose

❏ DEFINITION (WHO)

International Non-proprietary Name (INN): A unique, globally recognized name for a pharmaceutical substance or active pharmaceutical ingredient (API), designated by WHO. INN ensures safe prescribing and dispensing of medicines, avoiding confusion between brand names.

Also called: Recommended INN (rINN) — after WHO review. Previously: British Approved Name (BAN), United States Adopted Name (USAN), Japanese Adopted Name (JAN) — these have been largely harmonized under INN.

How INN System Works

1. Manufacturer/researcher applies to WHO for a new INN.
2. WHO Secretariat proposes a recommended name based on INN stems.
3. Proposed INN (pINN) published for public objection (4 months).
4. If no conflict → becomes Recommended INN (rINN).
5. Countries notify WHO of any conflicts with existing trademarks.
6. WHO publishes annually in 'WHO Drug Information'.

INN Stems — The Secret Code in Drug Names

INN stems reveal the drug class. Examiners LOVE these. Memorize the key ones:

Stem (suffix/prefix)	Drug Class	Examples
-olol	-olol = β -blocker	Atenolol, Metoprolol, Propranolol
-pril	ACE inhibitor	Enalapril, Lisinopril, Ramipril

Stem (suffix/prefix)	Drug Class	Examples
-sartan	ARB (Angiotensin Receptor Blocker)	Losartan, Valsartan, Candesartan
-statin	HMG-CoA reductase inhibitor	Atorvastatin, Rosuvastatin, Simvastatin
-oxacin / -floxacin	Fluoroquinolone antibiotic	Ciprofloxacin, Norfloxacin, Levofloxacin
-mycin / -micin	Aminoglycoside / Macrolide	Gentamicin, Azithromycin, Tobramycin
-cillin	Penicillin antibiotic	Amoxicillin, Ampicillin, Cloxacillin
-zole	Antifungal (azole) / PPI	Fluconazole / Omeprazole, Pantoprazole
-mab	Monoclonal antibody	Trastuzumab, Adalimumab, Rituximab
-nib	Tyrosine kinase inhibitor	Imatinib, Gefitinib, Erlotinib
-vir	Antiviral	Acyclovir, Tenofovir, Oseltamivir
cef- / ceph-	Cephalosporin antibiotic	Cefuroxime, Cephalexin, Cefixime

MNEMONIC — INN = "BOSS" Name: Brand name is the company's name, INN is the drug's real BOSS name that belongs to everyone!

Brand name: Calpol / Panadol / Tylenol / Dolo

INN: Paracetamol (one name, worldwide)

Importance in PV: ADRs should always be reported using INN to avoid confusion between different brand names in global databases like Vigibase®.

Importance of INN in Pharmacovigilance

- Allows global signal detection regardless of brand names.
- Prevents duplication in ICSR databases (same drug, different brands).
- Enables accurate DDD calculation and drug utilization studies.
- Supports cross-country pharmacovigilance collaboration.
- Mandated on all ICSR forms submitted to regulatory authorities.

DRUG DICTIONARIES AND CODING IN PHARMACOVIGILANCE

In pharmacovigilance, standardized drug dictionaries are used to code drugs in ICSRs, PSURs, and safety databases. Without a dictionary, the same drug might be entered in 100 different ways — making signal detection impossible.

WHO Adverse Reaction Terminology (WHO-ART)

❏ DEFINITION

WHO-ART: A structured medical terminology developed by WHO-UMC (Uppsala Monitoring Centre) specifically for coding adverse drug reactions in individual case safety reports (ICSRs). It was the ORIGINAL standard for ADR coding and has been largely replaced by MedDRA internationally, but is still used in some countries.

Feature	WHO-ART Details
Developed by	WHO-Uppsala Monitoring Centre (UMC)
Purpose	Standardized coding of ADRs in ICSRs
Structure	Hierarchical — 3 levels
Level 1 — SOC	System Organ Class (highest level) — e.g., 'Cardiovascular disorders'
Level 2 — Preferred Term (PT)	Specific medical term — e.g., 'Palpitations'
Level 3 — Included Term (IT)	Synonym / lay term — e.g., 'Heart racing'
Current status	Being phased out; MedDRA is now the global standard
Still used in	Some developing countries, older PV systems

MedDRA — Medical Dictionary for Regulatory Activities

▣ DEFINITION

MedDRA: The Medical Dictionary for Regulatory Activities (MedDRA) is a clinically validated, internationally standardized medical terminology developed under the International Council for Harmonisation (ICH) for use in regulatory communications and evaluation of data pertaining to medicinal products for human use.

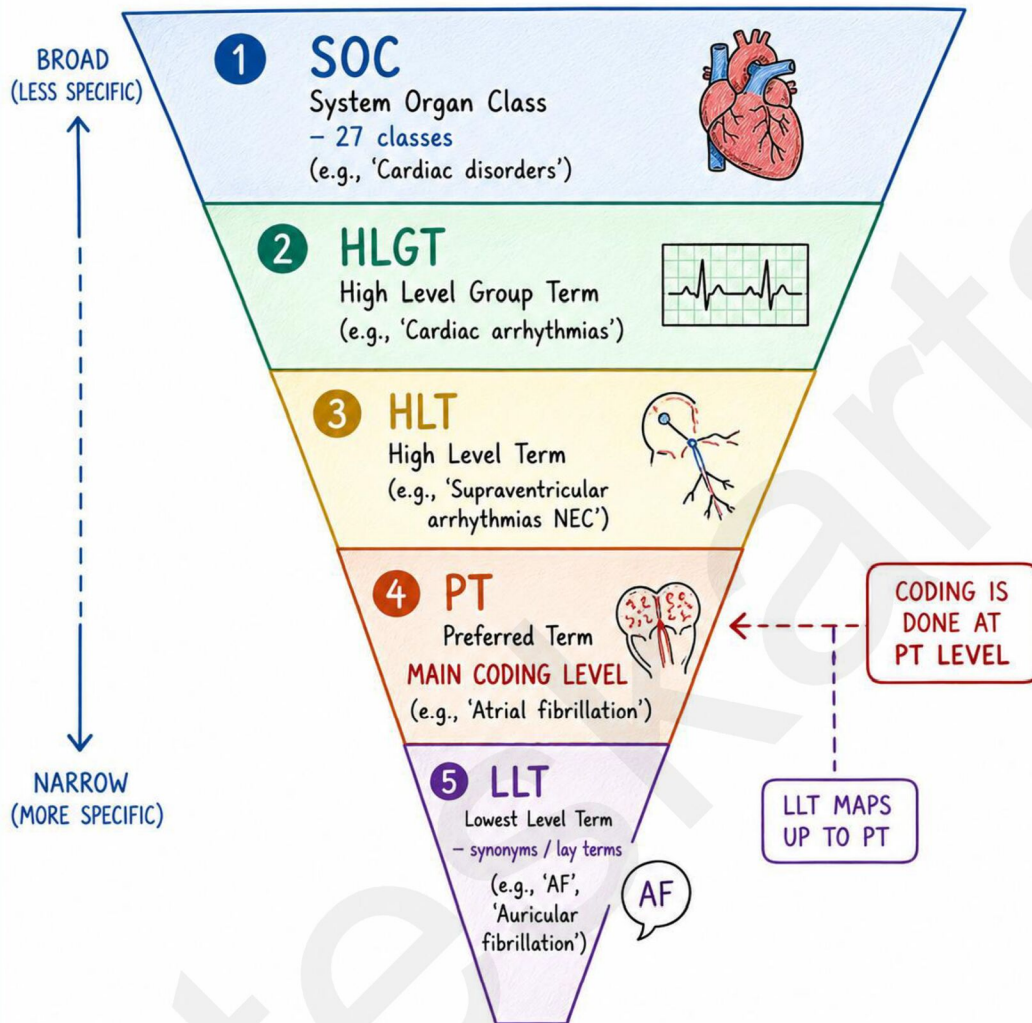
Maintained by: MedDRA MSSO (Maintenance and Support Services Organization) and PMDA (Japan)

Updates: Twice yearly — March and September. Current version: 27.0 (2024)

MedDRA Hierarchical Structure — The 5 Levels

MedDRA has 5 levels — from broadest to most specific. This is one of the MOST TESTED topics.

MedDRA FIVE-LEVEL HIERARCHY



MedDRA Level	Abbreviation	Description	Example (Liver ADR)	Count
1. System Organ Class	SOC	Broadest grouping by body system / etiology	Hepatobiliary disorders	27
2. High Level Group Term	HLGT	Groups of related HLTs	Hepatic and hepatobiliary disorders	~335
3. High Level Term	HLT	Groups of related PTs	Hepatocellular damage and hepatitis NEC	~1,730
4. Preferred Term	PT	Distinct medical concept — PRIMARY CODING LEVEL	Drug-induced liver injury	~24,400

MedDRA Level	Abbreviation	Description	Example (Liver ADR)	Count
5. Lowest Level Term	LLT	Synonyms, lay terms, older terms — maps to PT	DILI, hepatotoxicity due to drug	~79,000+

🔥 EXAM ALERT — MedDRA KEY FACTS

- There are **27 SOCs** in MedDRA (as of v27.0).
- Coding is done at **PT (Preferred Term)** level — NOT at LLT, HLT, HLGT, or SOC.
- LLTs are used for DATA ENTRY by the reporter, but system auto-maps to PT.
- MedDRA is MANDATORY for reporting to EMA, FDA (MedWatch), and most ICH-region regulatory authorities.
- MedDRA is NOT free — requires a license (free only for competent authorities and academia in some cases).

Standardized MedDRA Queries (SMQs)

📖 DEFINITION

Standardized MedDRA Queries (SMQs): Groupings of MedDRA terms related to a defined medical condition or area of interest used to support signal detection and safety data review.

SMQs are pre-defined groupings of MedDRA PTs and HLTs that together capture a complex medical concept — like 'anaphylaxis' or 'rhabdomyolysis' — that is too complex to capture with a single PT.

Feature	Details
Developed by	MedDRA MSSO, with input from regulatory agencies
Purpose	Facilitate signal detection, data retrieval across databases
Structure	SMQ contains MedDRA PTs grouped under a medical concept
Two types	Broad SMQ (sensitive — captures more, may have false positives) and Narrow SMQ (specific — fewer false positives)
Example SMQ 1	SMQ: Anaphylactic reaction — includes PT 'Anaphylaxis', 'Anaphylactic shock', 'Angioedema' etc.
Example SMQ 2	SMQ: Rhabdomyolysis/myopathy — captures statins' muscle ADRs
Example SMQ 3	SMQ: Drug-induced liver injury (DILI) — used in hepatotoxicity signal evaluation
Number of SMQs	~100+ currently defined
Application	PSUR signal detection, PBRER data analysis, regulatory queries

🔥 COMMON EXAM TRICK — SMQ

Question: What is the difference between PT and SMQ in MedDRA?

Answer: PT (Preferred Term) codes a single medical concept. SMQ is a **GROUPING** of multiple PTs and HLTs to capture a complex medical condition for safety analysis. SMQ is a tool for **QUERYING** data, not for coding ICSRs.

WHO Drug Dictionary (WHODrug Global)

📖 DEFINITION

WHO Drug Dictionary (WHODrug): A comprehensive multi-lingual pharmaceutical reference database maintained by UMC Uppsala that provides standardized drug names, ATC codes, formulations, and routes for use in pharmacovigilance databases. It is used to identify and code drugs on ICSRs.

Feature	Details
Maintained by	WHO-Uppsala Monitoring Centre (UMC)
Purpose	Standardized drug identification and coding in PV databases
Current version	WHODrug Global (successor to WHODrug-B and WHODrug-C)
Contains	INN, brand names, manufacturers, ATC codes, DDDs, formulations, routes, indications
Used in	VigiBase®, VigiFlow, clinical trial databases, hospital PV systems
Linked to	ATC/DDD system for drug utilization data
Updated	Quarterly
Languages	Multi-lingual — drug names in many languages
Use in ICSRs	Reporter enters brand name → WHODrug maps to INN → ATC code assigned automatically

EudraVigilance Medicinal Product Dictionary (EVMPD / XEVMPD)

DEFINITION

EudraVigilance: The European pharmacovigilance database and data-processing network managed by the European Medicines Agency (EMA) for collecting, managing, and analyzing reports of suspected adverse reactions to medicines authorized in the European Economic Area (EEA).

EVMPD / XEVMPD: The Extended EudraVigilance Medicinal Product Dictionary — a comprehensive database of medicinal products authorized in EEA, used to identify products in adverse reaction reports.

Feature	Details
Managed by	European Medicines Agency (EMA), Amsterdam
Database name	EudraVigilance (EV)
Drug dictionary	XEVMPD (eXtended EudraVigilance Medicinal Product Dictionary)
ICSR format	E2B (R3) — ICH format for electronic reporting
Public data portal	www.adrreports.eu — public access to European ADR data
Products covered	All medicines authorized in EU/EEA (centrally + nationally authorized)
Reporting by	MAHs, national competent authorities (NCAs), healthcare professionals
Timelines	Fatal/life-threatening SUSARs: 7 days; Others: 15 days

Comparison of Drug/ADR Dictionaries

Dictionary	Type	Maintained By	Purpose	Used For
WHO-ART	ADR terminology	WHO-UMC	ADR coding	Older PV databases
MedDRA	Medical terminology	ICH/MSSO	ADR, disease, procedure coding	Global regulatory submissions
SMQs	MedDRA query tool	ICH/MSSO	Signal detection	Data review, PSUR
WHODrug	Drug dictionary	WHO-UMC	Drug identification/coding	ICSRs, VigiBase®
XEVMPD	Drug product dictionary	EMA	EU drug product identification	EudraVigilance reporting
ICD-10/11	Disease classification	WHO Geneva	Disease/indication coding	ICSRs, drug utilization

INFORMATION RESOURCES IN PHARMACOVIGILANCE

Pharmacovigilance professionals need reliable drug safety information. Resources are of two types: (1) Basic drug information resources and (2) Specialized PV/ADR resources.

Basic Drug Information Resources

#	Resource	Publisher	Type	Key Use
1	Martindale: Complete Drug Reference	Royal Pharmaceutical Society, UK	Reference compendium	Drug monographs, formulations, indications, ADRs

#	Resource	Publisher	Type	Key Use
2	British National Formulary (BNF)	BMJ/RPS, UK	Prescribing guide	Drug selection, doses, ADRs, interactions
3	AHFS Drug Information	ASHP, USA	Reference	Comprehensive drug monographs
4	Drug Facts and Comparisons	Wolters Kluwer, USA	Reference	Therapeutic comparisons
5	Physicians' Desk Reference (PDR)	PDR Network, USA	Reference	US FDA-approved labeling (SPCs)
6	MIMS (Monthly Index of Medical Specialties)	Haymarket Media, India	India-specific	Widely used by Indian clinicians, drug index
7	Micromedex (DRUGDEX)	IBM Watson Health	Evidence-based	Drug-drug interactions, toxicity, evidence level
8	Clinical Pharmacology	Elsevier	Database	Detailed drug information, renal/hepatic dosing
9	Indian Pharmacopoeia (IP)	IPC Ghaziabad	Standards book	Drug standards, official India reference
10	Drugs@FDA	US FDA	Database	Approved US drugs, labeling, NDA data

Specialized Resources for ADRs in Pharmacovigilance

#	Resource	Maintained By	Key Feature
1	VigiBase®	WHO-UMC, Uppsala	Global ICSR database: 35+ million reports; public accessible via VigiLyze
2	FAERS (FDA Adverse Event Reporting System)	US FDA	US ADR database; public; replaced AERS; web-based query available at openFDA
3	EudraVigilance / adrreports.eu	EMA	European ADR database; publicly accessible, country-level data
4	MHRA Yellow Card database	MHRA, UK	UK ADR database; Yellow Card scheme; public reports available
5	CADRMP (Canada Vigilance ADR Online Database)	Health Canada	Canadian ADR reports
6	MedWatch	US FDA	Consumer/HCP voluntary ADR reporting portal for USA
7	VAERS (Vaccine Adverse Event Reporting System)	CDC + FDA, USA	US vaccine ADR database (AEFI)

#	Resource	Maintained By	Key Feature
8	Uppsala Reports	WHO-UMC	Quarterly newsletter — PV news, signal alerts
9	WHO Pharmaceuticals Newsletter	WHO Geneva	Drug safety communications globally
10	Pharmacovigilance Review (PVR) Journal	Academic	Peer-reviewed PV research
11	Drug Safety (Journal)	Adis/Springer	Top peer-reviewed journal for ADR research
12	British Journal of Clinical Pharmacology	Wiley	Pharmacology + PV research

Indian-Specific Information Resources

Resource	Details
PvPI official website	www.ipc.gov.in — ADR forms, reports, safety alerts from NCC Ghaziabad
CDSCO website	www.cdsc.gov.in — drug approvals, CDSCO safety alerts, banned drugs list
ADR PvPI Mobile App	Play Store app for submitting ADRs directly to PvPI
National Formulary of India (NFI)	IPC publication — covers Indian drug standards and formulations
CDAC (Centre for Development of Advanced Computing)	Indian health IT for drug safety databases
Pharmacovigilance Bulletin (PvPI)	Quarterly newsletter by IPC on ADR signals in India

ESTABLISHING A PHARMACOVIGILANCE PROGRAMME IN A HOSPITAL

Hospital PV is the MOST FREQUENTLY ASKED 10-mark topic in BP805ET. Learn this section like you are actually the hospital pharmacist tasked with setting it up. Practical understanding = exam excellence.

Rationale — Why Does a Hospital Need PV?

- Detect ADRs early in real clinical settings.
- Protect patients from preventable ADRs.
- Contribute data to national (PvPI) and global (WHO-UMC) databases.
- Fulfill regulatory obligations (NABH accreditation, CDSCO requirements).
- Promote rational drug use and reduce medication errors.

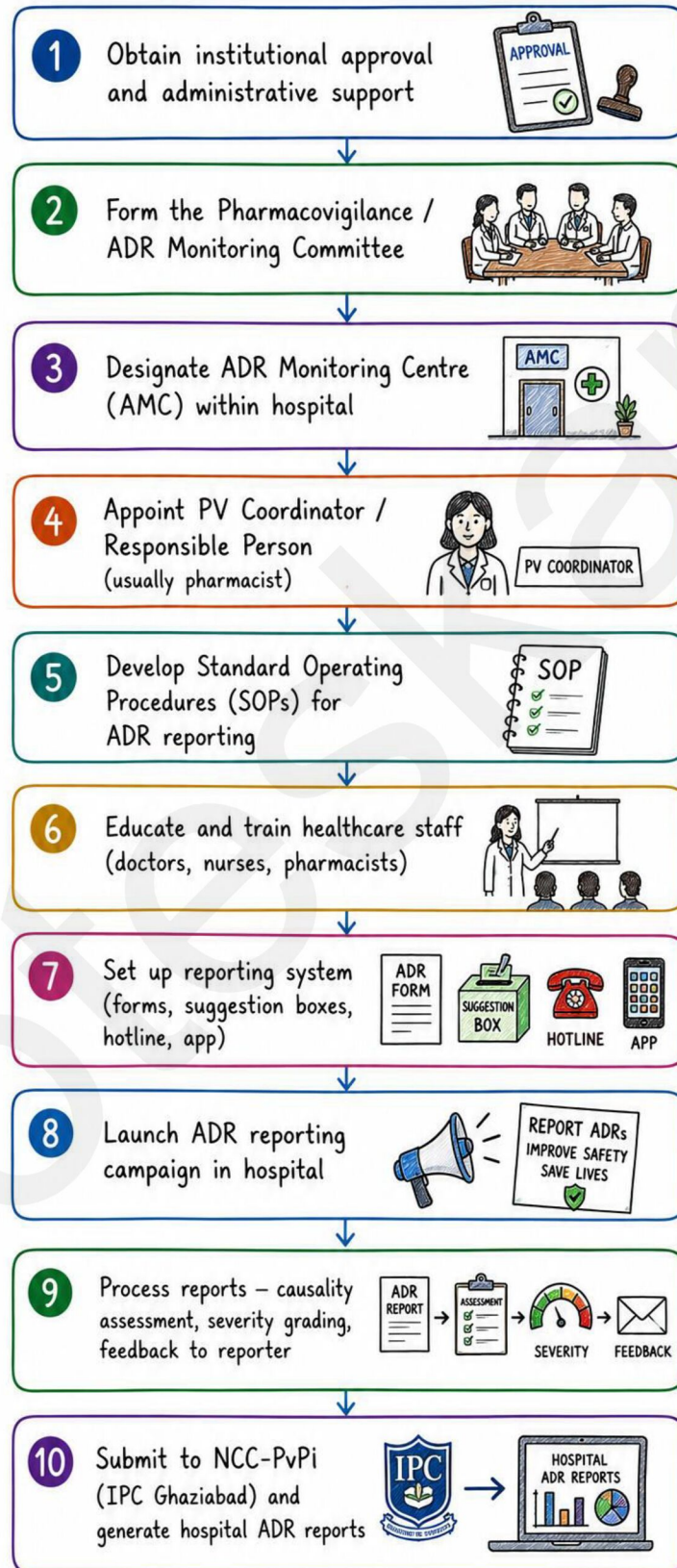
- Educational role — train doctors, nurses, pharmacists.

Prerequisites Before Starting

Prerequisite	What is Needed
Administrative support	Hospital management must formally endorse the programme
Legal framework	Awareness of PvPI guidelines, CDSCO rules, hospital pharmacy regulations
Dedicated personnel	Hospital pharmacist or clinical pharmacologist as PV coordinator
Physical infrastructure	ADR Monitoring Centre (AMC) office/space within pharmacy/clinical dept
Reporting forms	PvPI suspected ADR forms (red form for HCPs) stocked in all wards
Budget	For training, IT system, stationery, reporting software
Information system	Ideally electronic ADR tracking system (VigiFlow or hospital HIS)

Step-by-Step Process of Establishing Hospital PV

ESTABLISHING HOSPITAL PV PROGRAMME



Pharmacovigilance / ADR Committee

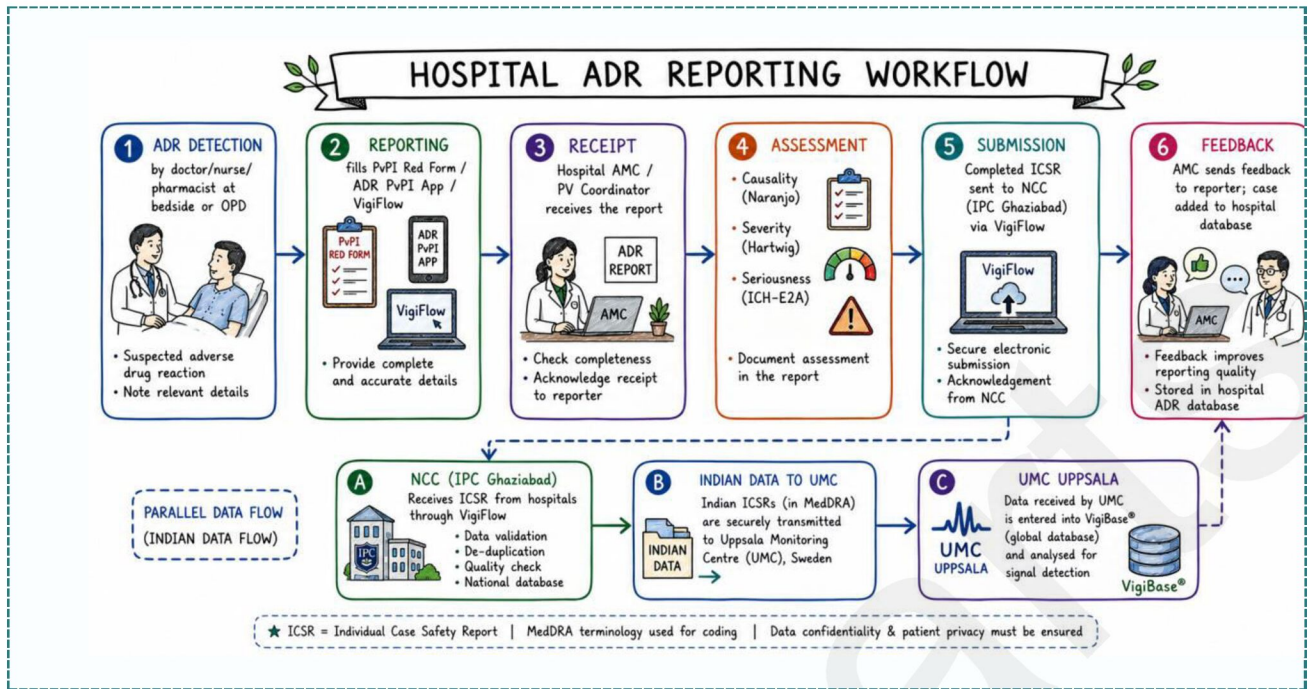
The PV Committee is the backbone of hospital pharmacovigilance. It is usually a sub-committee of the hospital's Pharmacy & Therapeutics Committee (P&T Committee).

Member	Role in PV Committee
Medical Superintendent / CMO	Chairperson; provides administrative authority
Clinical Pharmacologist / Physician	Clinical review of ADRs; causality assessment
Hospital Pharmacist (PV Coordinator)	Day-to-day operations; data management; reporting to PvPI
Nurse Representative	Bedside ADR detection and first-line reporting
Specialist Physicians (Cardiologist, Dermatologist etc.)	Expert opinion for specific ADRs (cardiac, skin)
Quality Manager	Process quality, NABH compliance
IT Representative	Database management, VigiFlow

Functions of Hospital ADR Monitoring Centre (AMC)

- Receive and process ADR reports from all hospital wards.
- Perform causality assessment (Naranjo / WHO-UMC scale).
- Perform severity and seriousness assessment (Hartwig / ICH-E2A).
- Send completed ICSRs to NCC-PvPI (IPC Ghaziabad) via VigiFlow.
- Provide feedback to the reporting HCP.
- Generate quarterly and annual ADR reports for hospital management.
- Conduct training sessions, CMEs on ADR reporting.
- Maintain confidentiality of patient and reporter data.
- Participate in signal detection activities.
- Maintain ADR database and formulary recommendations.

ADR Reporting in Hospital — The Workflow



Common Challenges in Hospital PV and Solutions

Challenge	Practical Solution
Under-reporting by HCPs	Regular training, incentivize reporting (recognition awards)
Lack of time for reporting	Simple 2-minute ADR app (ADR PvPI); bedside forms
Fear of medico-legal liability	Anonymous reporting option; confidentiality policy
Poor awareness of ADRs	Monthly CME, posters, newsletter
Inadequate IT infrastructure	Basic paper forms first; then VigiFlow
No dedicated PV coordinator	Assign responsibility to hospital pharmacist (Part-time initially)
No feedback to reporters	Send brief feedback within 7 days of receiving report

DRUG SAFETY DEPARTMENT IN PHARMACEUTICAL INDUSTRY

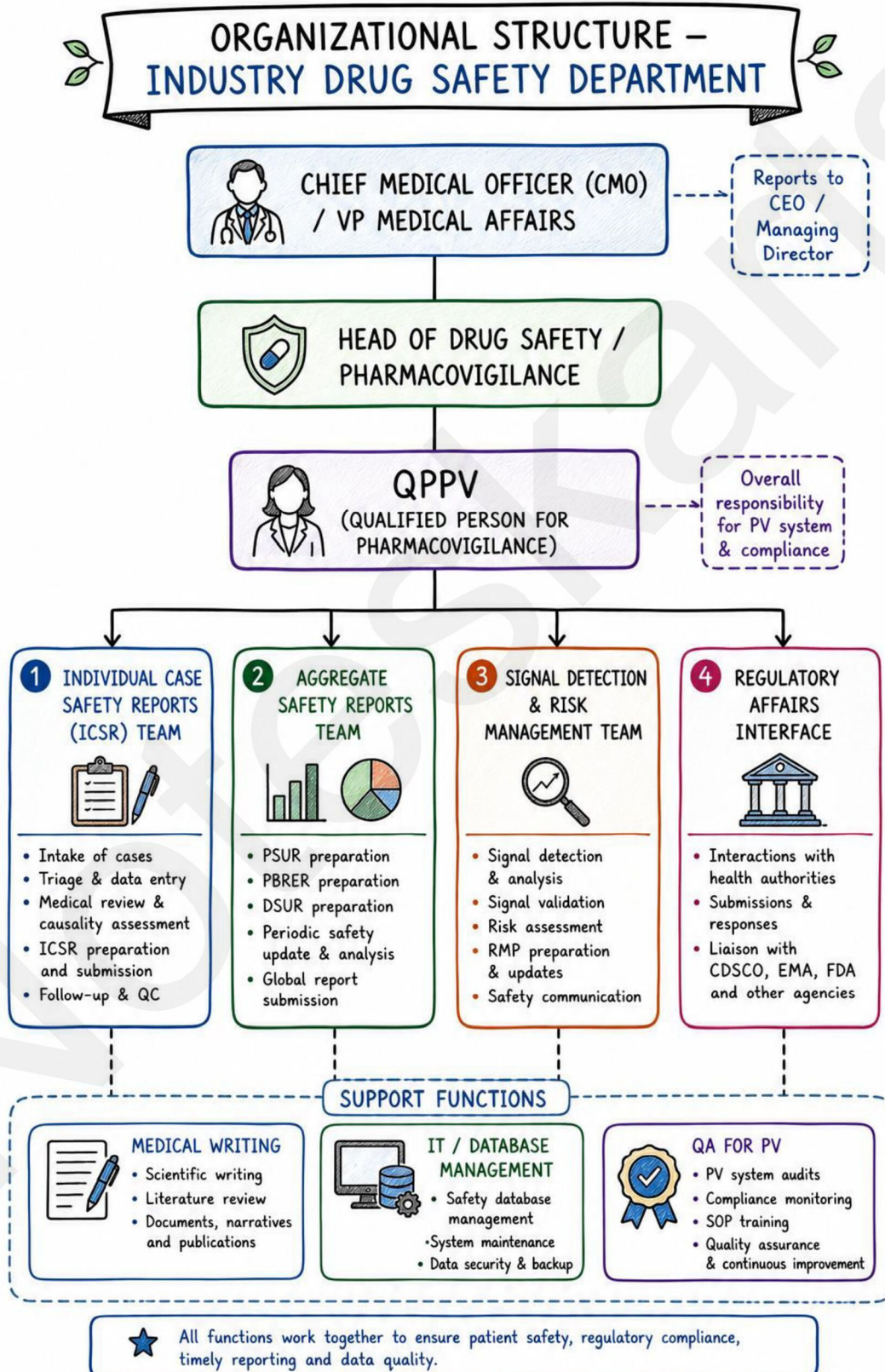
Every marketing authorisation holder (MAH) — a pharma company that has licensed a drug — is legally required to operate a drug safety department. In India, this is mandated under Schedule Y of Drugs & Cosmetics Act + CDSCO guidelines; globally under ICH-E2A to E2F.

Legal Obligations of MAH in Pharmacovigilance

- Maintain a complete pharmacovigilance system — may appoint a Qualified Person for Pharmacovigilance (QPPV).
- Collect, assess, and report all ICSRs (ADRs) from healthcare professionals, patients, clinical trials, and literature.
- Submit PSURs / PBRERs to regulatory authorities periodically.

- Maintain Risk Management Plans (RMPs) for all products.
- Update product labels (SmPC, package insert) as new safety data emerges.
- Issue Direct Healthcare Professional Communications (DHPCs) for urgent safety issues.
- Conduct Phase IV post-marketing studies if mandated.

Structure of Industry Drug Safety Department



Activities of Industry Drug Safety Department

Activity	Description	Regulatory Document
ICSR Management	Collect, assess, code (MedDRA), report ADRs within timelines	ICSR (E2B format)
Aggregate Reporting	Compile all safety data periodically into reports	PSUR / PBRER (ICH-E2C)
Signal Detection	Identify new safety signals using statistical methods (PRR, ROR)	Signal Assessment Report
Risk Management	Develop and maintain RMP; minimization activities	RMP (ICH-E2E)
Literature Surveillance	Monitor published literature (PubMed, Embase) for new ADRs	Manual/automated search (weekly)
Regulatory Reporting	Submit ICSRs and aggregate reports to CDSCO, EMA, FDA etc.	Various — country-specific
Label Management	Update Summary of Product Characteristics (SmPC) / package insert	Updated SmPC
Training	Train company staff on PV obligations	GVP Module I training records

ICSR Reporting Timelines for Industry (MAH)

Type of Report	Reporting Timeline	Clock Starts from
Fatal / Life-threatening SUSAR (Serious Unexpected Suspected ADR)	7 calendar days	Day Zero = MAH first receives information
Other Serious Unexpected ADRs (non-fatal/life-threatening)	15 calendar days	Day Zero
Serious Expected ADRs (labeled ADR)	15 days (or as per national requirements)	Day Zero
Non-serious ADRs	Included in PSUR (aggregate)	—
PSUR submission (new products)	Every 6 months for first 2 years post-launch	Regulatory authority schedule
PSUR submission (post-initial period)	Annually thereafter	—

EXAM TRICK — Reporting Timelines

Remember: 7-15-90 Rule in PV:

7 days → Fatal/Life-threatening SUSARs (expedited report)

15 days → Other SUSARs (expedited report)

90 days → Non-serious unexpected ADRs (periodic report) — (Note: some authorities differ)

Type of Report	Reporting Timeline	Clock Starts from
<p>Day Zero = The date MAH first receives the minimum information needed for a valid ICSR (patient, ADR, drug, reporter).</p>		

CONTRACT RESEARCH ORGANIZATIONS (CROs) IN PHARMACOVIGILANCE

❏ DEFINITION

Contract Research Organization (CRO): A company that provides outsourced drug development and pharmacovigilance services to the pharmaceutical, biotechnology, and medical device industries. CROs can take on all or part of the MAH's pharmacovigilance obligations under a formal contract.

PV Services Provided by CROs

PV Service	Description
ICSR Processing	Intake, triage, data entry, coding (MedDRA/WHODrug), causality assessment, regulatory submission
Aggregate Report Preparation	PSUR, PBRER, DSUR — writing, quality checking, regulatory submission
Signal Detection	Statistical and clinical signal analysis using VigiBase®, FAERS data
Literature Monitoring	Systematic weekly search of PubMed, Embase, local journals for new ADRs
Local Safety Officer Services	Providing a local contact person in countries where MAH has no office
QPPV Services	Some CROs supply a contractual Qualified Person for PV for smaller companies
Database/IT Management	Argus Safety, ARISg, Oracle Argus — industry PV databases
Training	GVP training for industry staff
Audit Support	PV audit preparation and response

Advantages and Disadvantages of CROs

Advantages of Using CRO	Disadvantages of Using CRO
Cost-effective — no need for large in-house PV team	Loss of direct control over PV activities

Advantages of Using CRO	Disadvantages of Using CRO
Access to specialized expertise (MedDRA coders, QPPV)	Communication/time-zone challenges
Scalable — can handle surge in ADR reports	Risk of data quality issues if CRO is poorly managed
Faster regulatory submissions (experienced team)	Contractual complexity and legal liability
Regulatory knowledge across multiple countries	Confidentiality and IP concerns
MAH remains legally responsible regardless of CRO	—

⚡ IMPORTANT — Legal Responsibility

Even when a CRO is used, the **MAH remains fully legally responsible** for all pharmacovigilance obligations. The CRO acts on behalf of MAH — it does NOT take over legal liability. This is a common exam MCQ!

PV Databases Used in Industry/CRO Settings

Database/Software	Developer	Use
Oracle Argus Safety	Oracle	Most widely used ICSR management system globally
ARISg	ArisGlobal	ICSR and PSUR management
Veeva Vault Safety	Veeva Systems	Cloud-based PV system
InForm	Oracle	Clinical trial ADR management
VigiFlow	WHO-UMC	National competent authority ICSR tool (free for members)
EVWEB	EMA	European ICSR submission portal

ESTABLISHING A NATIONAL PHARMACOVIGILANCE PROGRAMME

WHO has issued guidelines for countries to establish national PV programmes. Understanding this helps contextualize PvPI (India's national programme) and also appears directly in exam questions.

WHO Recommendations for a National PV Programme

According to WHO's 'Monitoring the Safety of Medicines: A Practical Manual for Developing Countries', a national PV programme requires:

Component	Requirement
Legal/Regulatory Framework	National drug law must mandate ADR reporting (in India: Drugs & Cosmetics Act, Schedule Y)
National Coordinating Centre (NCC)	Single national centre for PV coordination (India: IPC Ghaziabad)
Network of ADR Monitoring Centres	Hospitals and health facilities as primary collection points (India: 300+ AMCs)
Reporting System	Forms, hotlines, apps — accessible to HCPs and patients
Human Resources	Trained PV professionals at all levels
Database Management	Electronic ICSR database (VigiFlow in India)
Collaboration with WHO-UMC	Submission of national data to VigiBase®
Communication	Safety alerts, bulletins to HCPs (PvPI quarterly bulletin)
Funding	Government/regulatory authority budget allocation
Training & Education	Medical/pharmacy curricula to include PV (PCI mandated in B.Pharm syllabus)

Global Models of National PV Programmes

Country	Programme	Key Feature
India	PvPI (Pharmacovigilance Programme of India)	NCC at IPC Ghaziabad; 300+ AMCs; ADR PvPI app
USA	FDA MedWatch + FAERS	Voluntary + mandatory reporting; public database
UK	Yellow Card Scheme (MHRA)	Patient reporting pioneered; QR code on medicines
EU	EudraVigilance (EMA)	Centralized EU reporting; adrreports.eu public portal
Australia	Adverse Medicine Events (AME) — TGA	Consumer reporting via online form

Country	Programme	Key Feature
Canada	Canada Vigilance Programme — Health Canada	Bilingual (English-French) reporting
Japan	PMDA Reporting System	Highly structured; MedDRA mandatory
Sweden	UMC Uppsala (for WHO)	Global data custodian (VigiBase®)

PvPI as a National Programme — Complete Summary

IN PvPI COMPLETE SUMMARY (For 10-mark Questions)

Launch: 14 July 2010 | MoHFW, GoI

NCC: IPC, Ghaziabad (since 15 April 2011)

Regulatory Authority: CDSCO (Central Drugs Standard Control Organisation)

AMCs: 300+ across India (govt medical colleges + private)

Software: VigiFlow (since 2017)

Reporting forms: Red form (HCPs), Blue form (consumers)

Helpline: 1800-180-3024 (toll-free)

App: ADR PvPI (Play Store/App Store)

WHO membership: Official member since 1997; Indian data in VigiBase®

Scope: Allopathic + Ayush + Vaccines + Biologicals + Medical devices

Key Output: Quarterly PV Bulletin, Safety Alerts, Drug Safety Signals

IMPORTANT QUESTION BANK — UNIT II

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

Q1. Define ATC classification system.

Ans: ATC (Anatomical Therapeutic Chemical) classification system is an international WHO system maintained by Oslo Centre, Norway, in which drugs are classified into groups at 5 levels based on organ/system, and therapeutic, pharmacological, and chemical properties. Example: Metformin = A10BA02.

Q2. What is DDD? Give an example.

Ans: DDD (Defined Daily Dose) is the assumed average maintenance dose per day for a drug used for its main indication in adults, as defined by WHO. It is a unit of measurement for drug utilization studies, NOT necessarily the prescribed dose. Example: DDD of Metformin = 2 g oral.

Q3. What is INN? Give any 4 examples of INN stems.

Ans: INN (International Non-proprietary Name) is a unique WHO-designated global name for a pharmaceutical substance. Key stems: -olol (β -blockers), -pril (ACE inhibitors), -sartan (ARBs), -statin (HMG-CoA reductase inhibitors).

Q4. Differentiate between MedDRA and WHO-ART.

Ans: WHO-ART is the older ADR coding system by UMC (3 levels: SOC→PT→IT) now largely replaced. MedDRA is the current ICH-standard 5-level system (SOC→HLGT→HLT→PT→LLT) used for all regulatory submissions globally. MedDRA is more comprehensive and internationally mandated.

Q5. What are Standardized MedDRA Queries (SMQs)? Give an example.

Ans: SMQs are pre-defined groupings of MedDRA Preferred Terms (PTs) and HLTs related to a defined medical condition, used for signal detection and safety data queries. Example: SMQ for 'Anaphylactic reaction' groups PT 'Anaphylaxis', 'Anaphylactic shock', 'Angioedema' etc.

Q6. Name the MedDRA level at which ADR coding is done.

Ans: Coding in MedDRA is done at the Preferred Term (PT) level (Level 4). LLTs (Level 5) are used for data entry but are automatically mapped to PTs by the system.

Q7. What is EudraVigilance?

Ans: EudraVigilance is the European pharmacovigilance database and data-processing network managed by EMA (European Medicines Agency) for collecting, managing, and analyzing reports of suspected ADRs to medicines authorized in the EEA (European Economic Area).

Q8. What is a CRO in pharmacovigilance?

Ans: A Contract Research Organization (CRO) is a company providing outsourced PV services to pharmaceutical companies (MAHs). Services include ICSR processing, PSUR writing, literature monitoring, signal detection. Importantly, the MAH remains legally responsible even when a CRO is used.

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

Q1. Explain the ATC classification system with its five levels. Give the ATC code of Metformin with explanation of each level.

Q2. Describe MedDRA and its hierarchical structure. Add a note on SMQs.

Q3. Write a note on: (a) WHO Drug Dictionary (WHODrug Global) and (b) EudraVigilance

Q4. Describe the steps for establishing a pharmacovigilance programme in a hospital.

Q5. Explain the drug safety department in pharmaceutical industry. Describe ICSR reporting timelines.

PART C — 10-MARK QUESTIONS (3 Qs)

Q1. Define pharmacovigilance. Discuss the drug and disease classification systems used in pharmacovigilance including ATC classification, ICD-10, DDD, and INN with suitable examples.

Q2. Describe the drug dictionaries and coding systems used in pharmacovigilance. Discuss WHO-ART, MedDRA, SMQs, WHODrug, and EudraVigilance.

Q3. Discuss in detail how to establish a pharmacovigilance programme in a hospital and in the pharmaceutical industry. Add a note on CROs and national PV programme.

PREVIOUS-YEAR-STYLE QUESTIONS (5 Likely Qs)

PYQ-1 (10 marks)

Define pharmacovigilance. Explain the anatomical, therapeutic, and chemical classification of drugs with ATC classification system. Add a note on DDD and INN.

PYQ-2 (10 marks)

Discuss the drug dictionaries and coding systems in pharmacovigilance with special reference to MedDRA. Explain Standardized MedDRA Queries (SMQs).

PYQ-3 (5 marks)

Describe the establishment of a pharmacovigilance programme in a hospital. What is the role of the ADR Monitoring Committee?

PYQ-4 (5 marks)

Write a note on: (a) Contract Research Organizations in pharmacovigilance. (b) WHO Drug Dictionary.

PYQ-5 (2 marks each)

Short notes: (a) INN stems (b) ATC code of Aspirin (c) SMQ (d) Day Zero in pharmacovigilance

✓ TOP 25 EASY MCQs — UNIT II (with Detailed Explanations)

Q1. The ATC classification system is maintained by WHO Collaborating Centre in:

- A) Geneva, Switzerland
- B) Uppsala, Sweden
- C) Oslo, Norway**
- D) London, UK

Answer: C — ATC/DDD system is maintained by WHO Collaborating Centre for Drug Statistics Methodology in Oslo, Norway.

Q2. How many levels does the ATC classification system have?

- A) 3
- B) 4
- C) 5**
- D) 6

Answer: C — ATC has 5 levels: (1) Anatomical Main Group, (2) Therapeutic Main Group, (3) Therapeutic/Pharmacological Subgroup, (4) Chemical Subgroup, (5) Chemical Substance.

Q3. The ATC code of Metformin is:

- A) A10BA01
- B) A10BA02**
- C) N02BA01
- D) C07AB03

Answer: B — Metformin (biguanide antidiabetic) = A10BA02. Level breakdown: A (alimentary), 10 (diabetes drugs), B (excl. insulins), A (biguanides), 02 (metformin).

Q4. Aspirin used as an analgesic has ATC code:

- A) B01AC06
- B) N02BA01**
- C) A01AD05
- D) M01AE01

Answer: B — Aspirin as analgesic = N02BA01 (N=nervous system). Aspirin as antiplatelet = B01AC06 (B=blood). SAME drug, DIFFERENT ATC codes based on indication!

Q5. DDD stands for:

- A) Drug Defined Dose
- B) Daily Defined Dose
- C) Defined Daily Dose**
- D) Drug Dosage Determination

Answer: C — DDD = Defined Daily Dose. It is the assumed average maintenance dose per day for a drug's main indication in adults.

Q6. DDD of Metformin oral is:

- A) 500 mg
- B) 1 g
- C) 2 g**
- D) 3 g

Answer: C — WHO-assigned DDD for Metformin oral (A10BA02) = 2 g (standard adult maintenance dose for T2DM). This equals 500 mg QID = 2 g.

Q7. INN is designated by:

- A) FDA
- B) WHO**
- C) CDSCO
- D) ICH

Answer: B — *INN (International Non-proprietary Name) is designated by WHO, ensuring a unique globally recognized name for every pharmaceutical substance.*

Q8. Which INN stem indicates a beta-blocker?

- A) -pril
- B) -olol
- C) -sartan
- D) -statin

Answer: B — *-olol suffix = beta-blockers. Examples: atenolol, metoprolol, propranolol, carvedilol (partial β -blocker). -pril = ACE inhibitors; -sartan = ARBs; -statin = lipid-lowering.*

Q9. Which INN stem indicates a monoclonal antibody?

- A) -nib
- B) -vir
- C) -mab**
- D) -cillin

Answer: C — *-mab suffix = monoclonal antibody. Examples: trastuzumab (Herceptin), adalimumab (Humira), rituximab. -nib = tyrosine kinase inhibitors; -vir = antivirals.*

Q10. MedDRA was developed under which international body?

- A) WHO
- B) ICH**
- C) EMA
- D) FDA

Answer: B — *MedDRA was developed under ICH (International Council for Harmonisation) and is maintained by MSSO (Maintenance and Support Services Organization) and PMDA (Japan).*

Q11. How many System Organ Classes (SOCs) are in MedDRA?

- A) 18
- B) 22
- C) 27**
- D) 33

Answer: C — *MedDRA has 27 SOCs (System Organ Classes) as of MedDRA v27.0. This is a frequently tested number.*

Q12. MedDRA coding in ICSRs is done at which level?

- A) SOC
- B) HLGT
- C) HLT
- D) PT (Preferred Term)**

Answer: D — *Coding is done at the PT (Preferred Term) level — Level 4 in MedDRA. LLTs (Level 5) are for data entry only and auto-map to PTs.*

Q13. LLT in MedDRA stands for:

- A) Lower Level Terminology
- B) Lowest Level Term**
- C) Linked Level Term
- D) Lateral Level Term

Answer: B — LLT = Lowest Level Term — Level 5 (most specific) in MedDRA. It includes synonyms, lay terms, and older terms that all map upward to a PT.

Q14. Standardized MedDRA Queries (SMQs) are used for:

- A) Coding ICSRs
- B) Signal detection and data retrieval**
- C) Defining drug DDDs
- D) Classifying drugs in ATC

Answer: B — SMQs are pre-defined groupings of MedDRA terms used for SIGNAL DETECTION and safety data queries — NOT for coding ICSRs. Coding uses individual PTs.

Q15. WHO Drug Dictionary (WHODrug Global) is maintained by:

- A) WHO Geneva
- B) EMA
- C) Uppsala Monitoring Centre (UMC)**
- D) ICH-MSSO

Answer: C — WHODrug Global is maintained by UMC (Uppsala Monitoring Centre), Uppsala, Sweden. It links INN with ATC codes and is updated quarterly.

Q16. EudraVigilance is the pharmacovigilance database of:

- A) WHO
- B) US FDA
- C) EMA (European Medicines Agency)**
- D) ICH

Answer: C — EudraVigilance is EMA's European ADR database and data-processing network for collecting adverse reaction reports from EU/EEA countries.

Q17. The public portal for European ADR data is:

- A) openFDA
- B) adrreports.eu**
- C) VigiLyze
- D) MedWatch

Answer: B — adrreports.eu is EMA's public portal providing access to European ADR data. openFDA = US FDA data. VigiLyze = WHO-UMC VigiBase access.

Q18. An MAH is legally obligated to report a fatal SUSAR within:

- A) 7 days**
- B) 15 days
- C) 30 days
- D) 90 days

Answer: A — Fatal/life-threatening SUSARs must be reported within 7 calendar days of Day Zero (ICH-E2A). Non-fatal serious unexpected ADRs = 15 days. Non-serious = periodic (PSUR).

Q19. QPPV stands for:

- A) Qualified Person for Pharmacovigilance Practice
- B) Quality Policy for Pharmacovigilance
- C) Qualified Person for Pharmacovigilance**
- D) Quality Programme for PV

Answer: C — QPPV = Qualified Person for Pharmacovigilance — the EU-mandated responsible person within a pharma company who oversees all PV activities. Required under EU GVP.

Q20. When a CRO handles PV, the legal responsibility lies with:

- A) The CRO only
- B) The MAH only**
- C) Both CRO and MAH equally
- D) The regulatory authority

Answer: B — Even when PV is outsourced to a CRO, the MAH (Marketing Authorisation Holder) remains fully and legally responsible for all PV obligations. The CRO acts on MAH's behalf.

Q21. PvPI's current National Coordinating Centre is at:

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

Answer: B — IPC (Indian Pharmacopoeia Commission), Ghaziabad, UP has been the NCC since 15 April 2011. AIIMS was NCC only in 2010. Very common exam trap!

Q22. Which software is used for ICSR reporting by Indian AMCs to NCC-PvPI?

- A) Oracle Argus
- B) ARISg
- C) VigiFlow**
- D) EVWEB

Answer: C — VigiFlow is the WHO-UMC web-based ICSR management system adopted by PvPI/IPC since 2017 for Indian AMCs to report ICSRs to the national centre.

Q23. Which of the following is NOT a basic drug information resource?

- A) Martindale
- B) BNF
- C) VigiBase®**
- D) Micromedex

Answer: C — VigiBase® is a SPECIALIZED PV resource (global ICSR database at UMC). Martindale, BNF, and Micromedex are all basic drug information resources.

Q24. ICD-11 was effective from:

- A) January 2019
- B) January 2020
- C) January 2022**
- D) January 2024

Answer: C — ICD-11 (11th revision) was adopted by WHO in 2019 but became effective for use by member states from January 2022.

Q25. Which INN stem indicates an ACE inhibitor?

- A) -olol
- B) -sartan
- C) -pril**
- D) -dipine

Answer: C — -pril = ACE inhibitors (enalapril, lisinopril, ramipril, captopril). -olol = β -blockers; -sartan = ARBs; -dipine = calcium channel blockers (amlodipine, nifedipine).

All the best for your exam! 🎓

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