DEPTH OF BIOLOGY

Unit - 3

Clinical Trial Documentation- Guidelines to the preparation of documents, Preparation of protocol, Investigator Brochure,

Case Report Forms, Clinical Study Report Clinical Trial Monitoring-Safety Monitoring in CT

Adverse Drug Reactions: Definition and types. Detection and reporting methods. Severity and seriousness assessment.

Predictability and preventability assessment, Management of adverse drug reactions; Terminologies of ADR.

Clinical Trial Documentation

Clinical trial documentation refers to all the records, files, and documents that are created during the planning, conduct, and completion of a clinical trial.

These documents are important to:
Prove compliance with Good Clinical Practice (GCP) and regulations.
Ensure the safety and rights of participants.
Demonstrate the credibility and integrity of data.

According to ICH-GCP, essential documents are grouped into three stages:

1. Before the trial begins
2. During the trial
3. After completion/termination of the trial

Guidelines for Preparation of Clinical Trial Documents-

Clinical trial documents must be prepared according to ICH-GCP guidelines and local regulatory requirements.

They are called essential documents because they prove -

Protection of participants' rights and safety.

Compliance with Good Clinical Practice (GCP).

Reliability of trial data.

DEPTH OF BIOLOGY

General Guidelines for Preparation-

1. Clarity and Accuracy-
All documents should be clear, complete, and accurate.
Use simple, understandable language (especially for informed consent).

2. Standard Formats-
Prepare documents according to Standard Operating Procedures (SOPs) or sponsor-provided templates.
Maintain uniform style and terminology.

3. Review and Approval-
Documents must be reviewed and approved by appropriate authorities (Sponsor, Investigator, Ethics Committee, Regulatory Authority).
Approvals must be in writing and dated.

DEPTH OF BIOLOGY

4. Version Control -
Each document must have a version number and date.
Old versions should be archived, and only the current version used.

5. Signatures and Dates -
Essential documents (protocol, CRFs, agreements, consent forms) must be signed and dated by responsible persons (investigator, participant, sponsor).

6. Language Requirement-
Informed consent and patient information sheets must be in a local language understandable to participants.

7. Confidentiality-

Personal identifiers must be protected; use subject codes instead of names.

8. Compliance with Regulations-

Follow ICH-GCP, Declaration of Helsinki, Schedule Y (India), FDA, or EMA guidelines, depending on location.

9. Record Keeping-
Maintain documents in Trial Master File (TMF) for sponsor and Investigator Site File (ISF) for investigator.

Must be easily retrievable for monitoring, audits, or inspections.

10. Timeliness -
Prepare documents before trial starts, update during trial, and finalize after completion.
Safety reports and amendments must be submitted promptly.

DEPTH OF BIOLOGY

Examples of Key Documents-

Before trial → Protocol, Investigator's Brochure, Ethics Committee approval, Investigator CV, Insurance.

During trial → Informed consent forms, Case Report Forms (CRFs), SAE reports, monitoring reports, drug accountability logs.

After trial → Final study report, audit certificates, archival records.

DEPTH OF BIOLOGY

Launched by GCP & ICH.

CLINICAL TRIAL PROTOCOL

How to Conduct Clinical Trial.

Fixed Rules.

- It is a type of document in which we discuss that how to conduct the clinical trials, what are its objectives?, design? & methodology
- Clinical trial protocol is an important document to ensure the efficacy & safety of drug & to maintain integrity of documents
- This clinical trial protocol [rules & regulations] is launched by GCP & ICH
- GCP= good clinical practices & ICH= international council for harmonization
- GCP & ICH both release guidelines in which GCP. E6 (R2) : ICH. E6 (R1) contain

E6 → Section

(R2) → Guideline.

Information/fixed rules about clinical trials

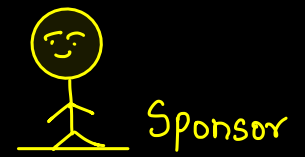
- Clinical trial protocols contain different document or different information

DEPTH OF BIOLOGY

1. GENERAL INFORMATION

- Related to investigational product [like which type of molecule category , drug profile, solubility , permeability] & its identification number

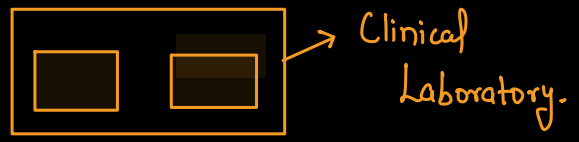
- Information about sponsor [name, address, mobile number]



- Information of approval authority who approved clinical trial protocol or who signed clinical trial protocol

- Information of scientific team
- Information of physician [to conduct clinical trial protocol we need a physician] - name, address & mobile number

- Information of Clinical laboratory where test is conducted



DEPTH OF BIOLOGY

2. BACKGROUND INFORMATION-

→ Total Information of Pre-Clinical Studies.

✓Here we submit all the information/data/document or report of pre-clinical studies

✓Like which method is used [route of administration, dose regimen], which animal is used for experiment etc

3. TRIAL OBJECTIVE & PURPOSE-

✓What is the purpose of medicine that has been manufactured or Formulate.

DEPTH OF BIOLOGY

4. TRIAL DESIGN-

✓How we can give dose to the subject

✓All the methods which are used to give drug to subject must be mentioned in trial design

5. SELECTION & WITHDRAWL OF SUBJECT: VOLUNTEER SELECTION & WITHDRAWL-

✓For conduction of successful clinical trial we have to select the subject/volunteer in which we perform clinical trials.

✓All the criteria/information must be mentioned here for selection or withdrawal of the subject

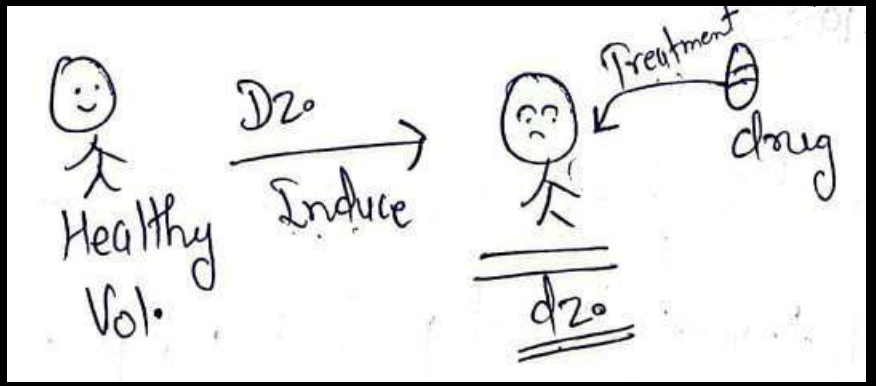
{many volunteer are required- like healthy/ unhealthy etc}

(Homogenous, Heterogenous).
or

DEPTH OF BIOLOGY

6. TREATMENT OF SUBJECT-

✓Disease is induced in an healthy subject/volunteer then the medicine is used to treat the subject with mentioned criteria



7. ASSESSMENT OF EFFICACY-

✓Mention the effective criteria for drug

✓How we can conclude effectiveness of drug

✓How we can calculate drug effectiveness

8. ASSESSMENT OF SAFETY-

✓Mention all the parameters, so we can conclude the clinical safety of drugs

DEPTH OF BIOLOGY

9. STATICS-

✓Mathematical representation of our result

10. DIRECT ACCESS TO SOURCE

✓Mention the reference of document

11. QUALITY CONTROL & ASSURANCE

12. FINANACE & INSURANCE

13. PUBLICATION POLICY

14. SUPPLEMENTS

Preparation of Clinical Trial Protocol-

Introduction-

A protocol is a written document that gives the complete plan of a clinical trial.

It describes why the trial is being done, how it will be carried out, who can participate, and what methods will be used to collect and analyze data.

It is considered the backbone of a clinical trial.

Steps for Preparation of Protocol-

1. General Information-

Title of the study, protocol number, version and date.
Name of sponsor, investigators, and trial sites.
Background about the investigational drug (chemical name, mechanism, past studies).

2. Objectives of the Trial-

Primary objective → main goal, like checking safety or effectiveness.
Secondary objective → other goals like effect on quality of life, side effects, or biomarkers.

DEPTH OF BIOLOGY

3. Study Design-

Type of trial (randomized, double-blind, open-label, crossover, etc.).
Number of groups/arms.

Duration of treatment and follow-up.

A simple diagram or flowchart may be included.

4. Study Population-
Inclusion criteria → who can take part (example: age, disease condition).

Exclusion criteria → who cannot take part (example: pregnant women, serious illness).

Total number of participants planned.

DEPTH OF BIOLOGY

5. Treatment Plan-
Details of investigational product: name, dose, route, frequency, duration.
Control or comparator (placebo or standard drug).
Randomization and blinding procedure.

6. Study Procedures-
What examinations and tests will be done at each visit.
Screening process, baseline investigations, follow-up visits, and final evaluation.
Laboratory tests, imaging, and physical examinations.

7. Safety Measures-
How to record and report Adverse Events (AEs) and Serious Adverse Events (SAEs).
Criteria for stopping treatment or withdrawing a participant.
Emergency procedures and medical management.

8. Data Collection and Management
How data will be recorded (Case Report Form – CRF).
Methods of data entry (paper or electronic).
Coding system for participant identity (to maintain confidentiality).

9. Statistical Analysis
Sample size calculation.
Statistical tests and methods to analyze primary and secondary outcomes.
Plan for interim analysis, if required.

10. Ethical Considerations
Statement that the trial will follow ICH-GCP guidelines and Declaration of Helsinki.
Requirement of Ethics Committee approval.
Process for obtaining informed consent.
Insurance and compensation policy for participants in case of trial-related injury.

DEPTH OF BIOLOGY

11. Monitoring and Quality Control

Role of sponsor and monitoring team.

Frequency of monitoring visits.

Handling of protocol deviations or violations.

Plan for audits and inspections.

12. Administrative Information

Publication policy and authorship.

Archiving and record retention.

References and appendices (Investigator's Brochure, consent form, patient info sheet).

DEPTH OF BIOLOGY

Investigator's Brochure (IB)-

Introduction

The Investigator's Brochure (IB) is a comprehensive document that contains all the pre-clinical and clinical information available on an investigational product (drug, vaccine, device, etc.).

It helps the investigator understand the rationale, safety, and proper use of the investigational product during a clinical trial.

It is prepared by the sponsor and updated regularly.

DEPTH OF BIOLOGY

Purpose of IB-

To provide scientific background for the trial.

To guide investigators on the safe and proper use of the investigational product.

To support risk–benefit assessment for participants.

To maintain consistency of information across multiple trial sites.

DEPTH OF BIOLOGY

Contents of Investigator's Brochure-

As per ICH-GCP guidelines, the IB should contain the following sections:

1. Title Page
Name of investigational product.
Identification number and version/date of the IB.
Sponsor's name and contact details.
Confidentiality statement.

2. Table of Contents
Easy navigation of all sections.

3. Summary
Brief overview of pre-clinical, clinical, and safety data.
Overall risk-benefit assessment.

DEPTH OF BIOLOGY

4. Introduction-
Background information about the investigational product.
Proposed indication and therapeutic area.
Rationale for clinical development.

5. Physical, Chemical, and Pharmaceutical Properties-
Chemical structure, molecular formula, physical description.
Solubility, stability, formulation details.
Storage conditions.

6. Non-Clinical Studies
Pharmacology: mechanism of action, animal studies.
Toxicology: acute, sub-chronic, chronic, carcinogenicity, reproductive toxicity studies.
Pharmacokinetics in animals (ADME: Absorption, Distribution, Metabolism, Excretion).

DEPTH OF BIOLOGY

7. Clinical Studies

Previous human experience (Phase I, II, or III studies).

Pharmacokinetics in humans.

Pharmacodynamics (effects on body systems).

Efficacy data (if available).

8. Safety and Adverse Events

Known side effects from earlier studies.

Dose-related toxicity and safety margins.

Precautions, warnings, drug–drug interactions.

9. Guidelines for Investigator

Recommended dosage and administration.

Route of administration.

Monitoring requirements during trial.

Management of overdose or adverse effects.

Case report forms

A Case Report Form (CRF) is a specially designed document (paper or electronic) used in a clinical trial.

It is used to collect data from each participating subject (patient or volunteer).

All clinical trial data required by the protocol is recorded on the CRF.

Purpose of CRF-

To ensure uniform data collection from all sites and participants.

To make sure that the data collected is relevant to study objectives.

To maintain accuracy, completeness, and consistency in trial records.

Acts as a source to transfer information from the trial site to the sponsor or regulatory body.

DEPTH OF BIOLOGY

Types-

Paper CRF (pCRF): Traditional method, data entered manually on paper forms.

Electronic CRF (eCRF): Computer-based data entry (more common now).

Advantages: faster, fewer errors, secure, easy to analyze.

#Characteristics of a Good CRF-

Simple and clear layout.
Protocol-driven (collects only what is needed for objectives).
Standardized (same for all participants/sites).
User-friendly (easy for site staff to fill).
Accurate and complete (all required data captured).
Compliant with regulatory requirements (ICH-GCP, FDA, EMA).

DEPTH OF BIOLOGY

Importance in Clinical Trials-

Ensures quality of data (data integrity, consistency, traceability).

Forms the primary source of data for statistical analysis.

Plays a major role in regulatory submission of trial results.

Used in audits and inspections by regulatory authorities.

Clinical Study Report (CSR)-

A Clinical Study Report is a complete, written description of a clinical trial.

It contains methods, conduct, results, and conclusions of the study.

It follows ICH-GCP and regulatory guidelines (like ICH E3).

A Clinical Study Report (CSR) is a comprehensive written document that provides the complete details of a clinical trial.

It is prepared after the completion of the trial.

DEPTH OF BIOLOGY

Purpose-

To present full and accurate results of the trial.

To provide information for regulatory authorities (e.g., FDA, EMA, DCGI).

To ensure transparency and credibility of the trial.

To allow scientific community and sponsor to analyze safety and efficacy of the drug.

To serve as a reference document for publications or further studies.

DEPTH OF BIOLOGY

Structure of a CSR (as per ICH E3)-

A. Front Section-

Title page → study title, protocol number, sponsor details.

Synopsis/Abstract → short summary of objectives, design, participants, results, and conclusions.

Table of contents.

B. Main Body-

1. Introduction – background and study objectives.

2. Study Design and Methods – trial type, randomization, blinding, number of subjects, inclusion/exclusion criteria.

DEPTH OF BIOLOGY

3. Study Population – demographics, medical history, baseline data.

4. Treatment and Procedures – drug dose, administration, duration.

5. Efficacy Evaluation – results showing effectiveness of the drug.

6. Safety Evaluation – adverse events, lab tests, vital signs, tolerability.

7. Statistical Methods and Results – data analysis and interpretation.

8. Discussion and Conclusion – overall benefit-risk assessment.

C. End Section-

References.
Appendices – protocol, CRFs, patient listings, investigator CVs, ethics approvals, monitoring reports.

DEPTH OF BIOLOGY

Importance of CSR-

Provides evidence of safety and efficacy of a new drug.

Acts as a legal and scientific document for drug approval.

Used in regulatory submissions (e.g., NDA, ANDA, IND reports).

Helpful in publication of study results in journals.

Useful for future research and meta-analyses.

Clinical Trial Monitoring-

1. Meaning-

Clinical trial monitoring is the process of overseeing the progress of a clinical trial. It ensures that the rights and safety of participants are protected, and that the trial data is accurate, complete, and verifiable.

Done by a monitor (Clinical Research Associate - CRA) on behalf of the sponsor.

Purpose of Monitoring-

To protect the safety and well-being of participants.
To ensure informed consent is obtained properly.
To verify that the trial follows protocol, SOPs, GCP, and regulations.
To check the quality and reliability of collected data.
To ensure proper drug handling, storage, and accountability.

DEPTH OF BIOLOGY

Responsibilities of a Monitor (CRA)-

Before Trial (Pre-trial visits):
Verify site facilities, staff, equipment.
Check approvals (ethics committee, regulatory authority).

During Trial (On-site or remote monitoring):
-Ensure subjects are eligible as per protocol.
-Confirm informed consent process.
-Compare Case Report Forms (CRFs) with source documents (medical records).
-Verify drug storage, labeling, accountability.
-Report and track protocol deviations/violations.
-Check for timely reporting of adverse events.
-Ensure essential documents are maintained in Trial Master File (TMF).

DEPTH OF BIOLOGY

After Trial (Close-out visit)-

Ensure study drug is returned/destroyed properly.

Confirm all documents are complete.

Prepare monitoring reports.

Types of Monitoring-

On-site monitoring – Physical visits to trial site.

Central/Remote monitoring – Review of trial data from sponsor's office using electronic systems.

Risk-based monitoring – Focus more on high-risk sites/data instead of routine checking everywhere.

DEPTH OF BIOLOGY

Importance of Clinical Trial Monitoring-

Ensures ethical conduct of the trial.

Maintains integrity and reliability of trial data.

Builds trust between sponsor, investigators, regulators, and public.

Helps in regulatory approval of new drugs.

Adverse Drug Reaction

An Adverse Drug Reaction (ADR) is a harmful or unwanted response to a drug that occurs at normal doses used for treatment, prevention, or diagnosis.

Unlike "side effects" (which may be mild and expected), ADRs are usually harmful, unintended, and unpredictable.

An ADR is a response to a drug which is noxious and unintended, and which occurs at doses normally used in humans."

Classification of ADRs

1. Type A (Augmented)-

Related to pharmacological action of the drug.
Dose-dependent and predictable.

More common
Example:
Hypotension with antihypertensives.
Hypoglycemia with insulin.
Bleeding with anticoagulants.

2. Type B (Bizarre)-

Unpredictable, not dose-related.
Due to allergy or genetic abnormality.
Less common but more dangerous.

Example:
Anaphylaxis with penicillin.
Steven-Johnson syndrome with sulfa drugs.

3. Type C (Chronic)-

Occur during long-term therapy.
Time- and dose-related.

Example:
Osteoporosis with corticosteroids.
Tardive dyskinesia with antipsychotics.

4. Type D (Delayed)-

Appear after a long time, even after stopping drug.

Example:

Carcinogenic effects of anticancer drugs.

Infertility from alkylating agents.

5. Type E (End of use / Withdrawal)-

Occur when a drug is suddenly stopped.

Example:

Seizures after sudden withdrawal of benzodiazepines.

Hypertension after stopping clonidine.

6. Type F (Failure of Therapy)-

Drug fails to give expected result.

May be due to drug interactions, resistance, or wrong dose.

Example:

Oral contraceptive failure with rifampicin (due to enzyme induction).

DEPTH OF BIOLOGY

Risk Factors for ADRs-

1. Patient factors

Age: children & elderly more sensitive.

Gender: women may react differently.

Genetic factors: G6PD deficiency → hemolysis with sulfa drugs.

Organ impairment: kidney/liver disease increases toxicity.

2. Drug factors

High dose or long-term use.

Narrow therapeutic index (e.g., digoxin, lithium).

Polypharmacy (use of many drugs at once).

3. Disease factors

Chronic diseases (diabetes, cancer, heart disease) may increase ADR risk.

DEPTH OF BIOLOGY

Detection of ADRs-

Clinical observation by doctors, nurses, or pharmacists.

Patient self-reporting (symptoms like rash, nausea).

Laboratory tests (e.g., abnormal liver/kidney tests).

Pharmacovigilance systems like:

Spontaneous reporting (yellow card system in UK, PvPI in India).

Hospital-based monitoring.

Post-marketing surveillance.

DEPTH OF BIOLOGY

Importance of ADR Monitoring-

Improves drug safety.
Helps detect rare and serious ADRs not seen in clinical trials.
Provides data for drug labeling, warnings, dose adjustments.
Prevents future harm to patients.
Strengthens public trust in medicines.

Examples of ADRs-

Aspirin → gastric bleeding.
Aminoglycosides → nephrotoxicity, ototoxicity.
Sulfonamides → Stevens–Johnson syndrome.
Clozapine → agranulocytosis.
Chemotherapy → hair loss, bone marrow suppression.

DEPTH OF BIOLOGY

Detection and reporting methods

Detection means finding or identifying possible ADRs in patients. ADRs can be detected by:

A. Clinical Methods-

1. Spontaneous Observation-

Doctor, nurse, or pharmacist notices symptoms after drug use.

Example: Rash after antibiotic.

2. Patient Self-reporting-

Patient complains of side effects (headache, dizziness, stomach upset).

3. Detailed History Taking-

Asking about drug use, timing, and symptoms.

Helps link the drug to the reaction.

4. Physical Examination-

Identifying visible signs (skin rash, swelling, jaundice).

DEPTH OF BIOLOGY

B. Laboratory Methods-

Routine Tests
Liver function tests → detect hepatotoxicity.

Kidney function tests → detect nephrotoxicity.

Specialized Tests-

ECG for arrhythmias.

Blood counts for drug-induced bone marrow suppression.

DEPTH OF BIOLOGY

C. Pharmacological / Statistical Methods-

-Prescription Event Monitoring (PEM)

Prescription data analyzed for unusual patterns.

-Cohort Event Monitoring-

Follow-up of patients taking a drug to note all events.

-Signal Detection (Data Mining)

Large-scale computer analysis of ADR databases (e.g., WHO-UMC, FDA).

Reporting of ADRs-

Once detected, ADRs should be documented and reported properly.

A. Spontaneous Reporting System-
Healthcare professionals fill ADR forms and send to national pharmacovigilance centers.
Example: Yellow Card System (UK), MedWatch (USA), PvPI (India).

B. Voluntary Reporting-
Doctors, nurses, pharmacists, or patients voluntarily report ADRs.

C. Mandatory Reporting-
Certain ADRs (e.g., Serious Adverse Events in clinical trials) must be reported within a fixed time (usually within 24 hours).

D. Hospital-based Monitoring-

Hospitals have ADR monitoring centers where staff collect and record ADRs.

E. Post-Marketing Surveillance (PMS)-

Continuous monitoring of drugs after launch in market to detect rare ADRs.

F. International Reporting-

National data forwarded to WHO-Uppsala Monitoring Centre (UMC), Sweden.
Maintains global ADR database (VigiBase).

DEPTH OF BIOLOGY

Importance of Detection & Reporting-

Helps identify rare or unexpected ADRs.

Improves drug labeling and safety warnings.

Protects patients from harm.

Strengthens pharmacovigilance system.

Provides data for regulatory decisions (suspension, withdrawal of unsafe drugs).

Severity and Seriousness Assessment of ADRs

Severity → The intensity or grade of the adverse reaction.

Seriousness → The regulatory classification based on the outcome of the adverse reaction.

Both are used in pharmacovigilance to evaluate ADRs, but they are not the same.

2. Severity Assessment-

Refers to how bad or strong the reaction is.
Describes clinical intensity (not the outcome).
Grading of Severity (CTCAE scale commonly used)

Mild (Grade 1)-
Symptoms are minor, do not interfere with normal activity.
Example: Mild nausea, slight headache.

Moderate (Grade 2)-
Symptoms interfere with daily activities, may need minimal treatment.
Example: Hypotension needing IV fluids.

DEPTH OF BIOLOGY

Severe (Grade 3)-

Symptoms are intense, disabling, require medical intervention.

Example: Severe rash, high fever.

Life-threatening (Grade 4)

Immediate risk of death without urgent intervention.

Example: Anaphylaxis, cardiac arrest.

Death (Grade 5)

Patient dies due to the ADR.

DEPTH OF BIOLOGY

-Seriousness Assessment-

Used for regulatory reporting of ADRs.
A reaction is serious if it results in:

1. Death.
2. Life-threatening condition.
3. Hospitalization (new or prolonged).
4. Disability/incapacity (significant or permanent).
5. Congenital anomaly/birth defect.
6. Any other medically important condition (e.g., arrhythmia needing urgent treatment).

DEPTH OF BIOLOGY

Importance-

Ensures patient safety by early recognition of dangerous ADRs.

Guides treatment decisions (continue, stop, or modify drug).

Essential for pharmacovigilance reporting and regulatory action.

Helps improve drug labeling and warnings.

Predictability and Preventability Assessment of ADRs

1. Predictability Assessment-
This tells us whether an ADR can be expected or not from the drug's action.

A. Predictable ADRs-
These ADRs are expected because they come from the known action of the drug.
They are usually dose-related.

They are more common.

Example:
Insulin → low blood sugar (hypoglycemia).
Warfarin → bleeding.
predictable ADRs can often be controlled by changing the dose or monitoring the patient.

B. Unpredictable ADRs-

These ADRs are unexpected and not related to the known action of the drug.

They are not dose-related and usually rare but serious.

Often due to allergy, genetics, or unusual patient response.

Example:
Penicillin → sudden anaphylaxis.

Sulfonamides → Stevens-Johnson syndrome.

Unpredictable ADRs are hard to prevent and may only be seen after many people use the drug.

DEPTH OF BIOLOGY

2. Preventability Assessment-

This tells us whether the ADR could have been avoided or not.

A. Definitely Preventable ADRs-
ADR happens because of a clear mistake in treatment.
Example: Giving penicillin to a patient who already has a known allergy.

B. Probably Preventable ADRs-

ADR might have been avoided with better care.
Example: Kidney damage from aminoglycosides if kidney tests were not monitored.

C. Not Preventable ADRs-
ADR occurs even if everything was correct.
Example: A person with no allergy history suddenly develops anaphylaxis after penicillin.

Management of adverse drug reactions

Management of ADRs means detecting, treating, preventing, and reporting harmful drug reactions to protect patients and improve drug safety.

Steps in Management of ADRs-

A. Recognition and Early Detection-

Careful observation of symptoms, patient history, and drug timing.

Use laboratory investigations if needed (e.g., liver/kidney function tests).

Confirm whether the problem is due to the drug (causality assessment).

DEPTH OF BIOLOGY

B. Immediate Management-

1. Stop or withdraw the suspected drug if possible.

2. Provide symptomatic treatment:
Antihistamines for rashes.
Anti-emetics for nausea.

3. Give emergency treatment if life-threatening:
Epinephrine and corticosteroids for anaphylaxis.
Oxygen and IV fluids for shock.

4. Use antidotes if available:
Naloxone for opioid toxicity.
Vitamin K for warfarin-induced bleeding.

C. Specific Management According to ADR Type-

Type A (Predictable, dose-related) → Reduce dose, monitor drug levels, adjust therapy.

Type B (Unpredictable, allergic/idiosyncratic) → Stop drug permanently, treat allergy, avoid re-exposure.

Chronic ADRs (Type C/D) → Regular monitoring, switch to safer alternatives if possible.

Withdrawal ADRs (Type E) → Gradual tapering instead of sudden stoppage.

DEPTH OF BIOLOGY

D. Prevention of Future ADRs-

Record the ADR in the patient's medical notes.

Educate the patient (e.g., carry allergy card/bracelet).

Use safer alternatives when prescribing next time.

Monitor high-risk drugs (like digoxin, lithium, aminoglycosides).

-Goals of ADR Management-

-Protect patient safety and life.
-Provide proper treatment of ADRs.
-Prevent recurrence of the same reaction.
-Generate data for pharmacovigilance and regulatory actions.
-Ensure safe and rational use of medicines.

Terminologies of ADR

1. Adverse Drug Reaction (ADR)-

A harmful or unpleasant response to a drug at normal doses, used for prevention, diagnosis, or treatment.

Example: Rash after taking amoxicillin.

2. Adverse Event (AE)-

Any untoward medical occurrence in a patient who has received a drug, not necessarily caused by the drug.

Example: Fever occurring during antibiotic therapy (may or may not be due to the drug).

3. Serious Adverse Event (SAE)-

An adverse event that results in:

Death,
Life-threatening situation,
Hospitalization (new or prolonged),
Disability or permanent damage,
Congenital anomaly,
Or other medically important condition.

4. Side Effect-

Any secondary effect of a drug that is related to its normal pharmacological action.
May be beneficial or harmful.
Example: Drowsiness with antihistamines.

5. Unexpected Adverse Reaction-

An ADR that is not consistent with current information in drug labeling, Investigator's Brochure, or product insert.

6. Idiosyncratic Reaction-

An unusual, abnormal, or genetically determined reaction to a drug.

Example: Hemolysis in G6PD-deficient patients after taking primaquine.

7. Allergic Reaction (Hypersensitivity)-

An immune-mediated response to a drug.

Example: Anaphylaxis with penicillin.

DEPTH OF BIOLOGY

8. Causality Assessment

The process of determining whether a drug is actually responsible for the reaction.
Methods: WHO-UMC system, Naranjo's scale.

9. Pharmacovigilance

The science and activities related to detecting, assessing, understanding, and preventing ADRs and other drug-related problems.

10. Signal Detection

Information that arises from one or more ADR reports suggesting a new possible association between a drug and an adverse event.

11. Risk Factors for ADRs-

Conditions that make a person more likely to experience an ADR, such as age, gender, genetics, organ disease, polypharmacy.

12. Black Box Warning-

The strictest warning by regulatory authorities (like FDA) for drugs that may cause serious or life-threatening ADRs.