INTRODUCTION TO PHARMACOLOGY

Recommended Books

Katzung B G. Basic and clinical pharmacology 12th Edition (New York) Mc Graw Hills

Board review series – **Katzung's & Trevor's ---**

Howland pilchard D. , Mary J. Mycek **Lippincott's** Illustrated reviews Pharmacology 6th Edition

Pharmacology

Greek; ***Pharmacon***

(an active principle)

&

logos *(*a discourse or treatise)

Pharmacology

A science which deals with the study of **substances** that interact with living systems &

activating or inhibiting normal body process

Therapeutics

The branch of medicine concerned with the **treatment of disease**

Therapy ---**the act of caring for someone** (as by medication or remedial training)

Physiotherapy ---- Therapy that **uses physical agents**: exercise, massage, & other modalities

Pharm; Pertaining to drug

Pharmacy --- The art of preparing or compounding and dispensing of medicines or preparing suitable dosage forms for administration of drugs to man or animals.

A **shop** for compounding and dispensing drugs and medical supplies

Pharmacist --- A qualified person licensed to compound or dispense drugs

Pharmaceutics -- The large scale manufacture of drugs

Pharm; Pertaining to drug

Pharmacognosy ---- identification of drugs

The study of biological, biochemical and economic features of natural drugs and their constituents

Materia medica -------

The science of drug preparation and the medical use of drugs.

Pharm; Pertaining to drug
Pharmacogenomics: (Pharmacogenetics)
The study of **genetic variations** that cause differences in drug response among individuals or populations.
Pharmaco-diagnosis --- The use of drugs in diagnosis
Posology--- It is the branch of pharmacology which deals with the **doses** of drugs
Pharm; Pertaining to drug
Pharmacogenomics: (Pharmacogenetics)
The study of **genetic variations** that cause differences in drug response among individuals or populations.

Pharm; Pertaining to drug
Pharmaco-diagnosis --- The use of drugs in diagnosis
Posology--- It is the branch of pharmacology which deals with the **doses** of drugs
Toxicology
(Greek; toxicos-poisonous; logos- discourse in)
That branch of pharmacology which deals with the **undesirable effects of drugs and chemicals** on living system
Detection, prevention
& treatment of poisoning

PHARMACOKINETICS
(Greek: Kinesis- movement)
It is the actions of **body on the drug**
What happens with the drug in the body (**absorption, distribution, metabolism,** and **excretion**)

PHARMACDYNAMICS
(Greek: dynamis - Power)
It is the actions of **drugs on the body**
Pharmacological effects --- therapeutic / toxic effects produced by the drug and its mechanism of action
Pharmodynamics
is what drugs do to the body
Pharmokinetics
is what the body does to drugs

Pharmacodynamics **Pharmacokinetics**
Where it acts? (site of action)
What are the effects ? (pharmacological effects)
How it acts? (mechanism of action)
Absorption (locally or into the blood from its site of application)
Distribution (to its site of action or other non required sites)
Permeation (through various membranes)
Elimination by **Metabolism** or **Excretion**

Drug
Any substance used for the purpose of diagnosis, prevention, relief or cure of a disease in man or animal
Drug (WHO, 1966)
"drug is any substance or product that is used or intended to be used to modify or explore physiological systems or pathological states for the benefit of the patients"

Drug
A chemical substance of known structure, other than a nutrient or an essential dietary ingredient, which, **when administered to a living organism, produce a biological effect.**

Drugs
A **drug** is any substance that brings about a **change in biological function** through its chemical actions. It reacts with a **regulator molecule called as receptor** to show its effects
Nature of drugs

Are hormones drugs?

Yes or No?

Hormonesare drugs synthesized within the body

Nature of drugs
Xenobiotics
(*Greek xenos; stranger*)
Chemicals not synthesized in the body
Drugs synthesized in the pharmaceutical industries
Poisons and Toxins
Poisons are substances that have almost exclusively harmful effects

Inorganic poisons --- lead, arsenic

Toxins are poisons of biological origin ---synthesized by plants or animals.

Are poisons drugs?

Yes or No?

Poisons in small doses are drugs

Paracelsus (1493-1541)

"All things are poisons and there is nothing that is harmless, **the dose alone** decides that something is no poison"

William withering (1741-1799)

"Poisons in small doses are the best medicine; and useful medicines in too large doses are poisonous" i.e., **drugs are useful poisons.**

Rumi's definition of poison

Anything which is more than our necessity is poison. It may be power, wealth, hunger, ego, greed, laziness, love, ambition, hate, or anything

Medicine / Drug

Medicine = active ingredient + excipient

A **drug** is a single chemical substance that forms the **active ingredient** of a medicine

Excipient

Substances in which an active ingredient (drug) is incorporated to formulate medicines

An **inert** (or slightly active substance) used in preparing medicines as a **vehicle or medium of administration** for the medicinal agents

Excipient

To deliver drugs in a stable form, acceptable and convenient to the patient

May affect absorption as well as solubility of the medicine

Lactose, sucrose, starch, calcium phosphate or lactate

Hippocrates (460-355 B.C.)

"First do no harm"

"It is good remedy sometimes to use nothing"

Napoleon Bonaparte, 1820

I do not want two diseases ----------

one nature made,

one doctor made

NOMENCLATURE OF DRUGS

Any drug has **three names**

Full chemical name
Non-proprietary
(official or approved)
Generic name
Proprietary name
(brand name, trade name)
Code name
RO 15-1788 (later named flumazenil)
Full chemical name
It describes the chemical (molecular) structure of the drug.
It is **unsuitable for prescription**
4-buty-3, 5-dioxo-1, 2- diphenylpyrazolidine
3-(10,11-dihydro-5H-dibenz[b,f]-azepin-5-yl)
Acetyl-p-aminophenol
1-(Isopropylamino)-3-(1-naphthyloxy) propan-2-o1 (propranolol)
Official or approved
(Non-proprietary) Generic name
United States Adopted Name **(USAN)** Council
r INN (Recommended international nonproprietary name)
Older drugs --- more than one name
Mepridine (USA), **Pethidine**(UK)
Metaproterenol (USA), **Orciprenaline** (UK)
Official or approved(Non-proprietary)
Generic name
Non-proprietary name ---- until the drug is included in a pharmacopoeia
Official name ---- after official publication in pharmacopoeia
Phenylbutazone, Imipramine, Paracetamol
It is usually the abbreviated form of the chemical name

Generic name
Often misused to mean as **non-proprietary name**
It refer to a **chemical or pharmacological group (or genus) of compound** e.g., barbiturates, suphonamide, phenothiazines, tricyclic antidepressants (TCA)
Nonproprietary name
Distinct in sound and spelling
Freedom from confusion with other drugs
Indicating relation between similar substance

Benzodiazepines
Diazepam, Nitrazepam, Flurazepam
ß-blockers
Propranolol, Atenolol, carvedilol, Ismolol

Proprietary name
(Brand name, trade name)
Trademark (the drug's proprietary **trade name)**
The name given by the company which markets the drug.
It is the commercial property of a pharmaceutical company
Several companies market the same drug under different proprietary names --- Valium, Mogadon, Dalmane
Acetaminophen (paracetamol) – colpol, panadol, disprol
Chemical name
Acetyl-p-aminophenol
Official name --- **Paracetamol**
Proprietary name
Calpol
Panadol
Disprol

Phenylbutazone
4-buty-3, 5-dioxo-1, 2- diphenylpyrazolidine
Phenylbutazone
Butazolidine, butacote, butazone, flexazome
Imipramine
3-(10,11-dihydro-5H-dibenz[b,f]-azepin-5-yl))
Imipramine
Tofranil

PLACEBO

Placebo (*Latin*, I will Please)
A dummy medicine containing no active ingredient, which the patient believes is the real drug
What are characteristics of a placebo?
An inert substance
No pharmacological action
Used as dummy drug

Made to appear identical with the active drug
Patient believes it to be the real drug
Purposes of use of Placebo
Used as control in scientific evaluation of drugs during clinical trial ---
Double blind technique
Placebo effect -- 'placebo response'
To benefit or to please a patient
given to satisfy patient **symbolic need** (**psychic need**) for dug therapy
A significant beneficial therapeutic effect -- Benefit the patient by psychological means
Useful in mild psychological disorders
Alleviation of the symptoms may be temporary
DRUG GROUPS

Drug groups
Impractical goal & **fortunately un-necessary** to learn each pertinent fact about individual drug
Several thousand drugs arranged in about **70 groups.**
In a group there is one or more **prototype** drugs and other classified as **variants** of the prototype
PROTOTYPE DRUGS
Typify the most important characteristics of the group
Only the **prototype must be learned in detail** and for the other remaining drugs (variants), only the differences from the prototype
Prodrug
The chemicals which needs some **metabolic conversion in the body before becoming an active pharmacological agent**
Methlydopa, an antihypertensive is first converted into alpha methylnorepinephrine to produce its pharmacological effects
Orphan drug
A drug for a rare disease ---
< 200,000 people in USA
Study and development is neglected
Sale is uncommon, might not pay the cost of development
To encourage the development of such a drug
Tax relief and other incentives are given by the government
Me-too drugs /products
A product created by a company that is similar to a competitor's product.

It is usually produced by simple chemical alteration of pharmacokinetic properties of the original drug making an i**dentical formulation**

Drugs and prescription

OTC (over the counter) **drugs --** Non-prescription

Safe & effective in treating common ailments

May interact with the prescription medication

OTC may be misused or abused

Prescription drugs

Restricted to **sale by prescription only ---** Prescription by a licensed prescriber

Controlled drugs -- Drugs with **abuse potential** include opioids, hallucinogens, stimulants

Nature of drug

The physical nature of drugs

Organic --- proteins, lipids, carbohydrates or

Inorganic --- iron, lithium, Iodine

Physical nature determine the best **route of administration**

Solid at room temperature – aspirin, atropine

Liquid --- Nicotine, Ethanol

Liquid & evaporate ---- halothane, amyl nitrate

Gaseous --- Nitrous oxide

Size of a drug molecule

Very small (lithium ion MW 7) to very large (alteplase (t-PA) MW 59050)

Majority of drugs MW between 100 to 1000

Route of administration &

Ability to move within the body from the site of administration to site of action

Very large drugs (usually proteins) directly administered into the compartment of action ---altepase -- I/V

Aqueous & Lipid Solubility

Weak bases or weak acids

The aqueous solubility --- degree of ionization or polarity of the molecule.

Water molecules behave as dipoles & are attracted to charged molecules, forming an aqueous shell around them.

The lipid solubility of a molecule is inversely proportional to its charge.

What drugs can do?

Drugs alter (activate or inhibit) **the normal functions of cells and tissues in the body**

Drugs cannot confer any new function on them

How drugs act?

Through Specific **receptors**

Alteration of the activity of **enzymes**

Nonspecific **chemical or physical** interactions -- Antacids, osmotic agents, and chelators

Antimetabolite action --- Drug **act as nonfunctional analogue** of a naturally occurring metabolite

Shape of Drug molecule

Shape --- permit binding to its receptor site

Drug reacts with a **regulator molecule called as receptor** to show its effects

What are receptors?

Receptors are **Protein molecules** whose function is to recognize & respond to endogenous chemical signals

Drug + Receptor ↔ drug-receptor complex → Effector molecule → biological effects

Other macromolecules with which drugs interact to produce their effects are known as **drug targets**

How drugs bind with the receptors?

Drugs interact with receptors by means of chemical forces or bonds

Covalent

Electrostatic

Hydrophobic

Covalent

(Very strong , may be irreversible)

Phenoxybenzamine & α adrenergic receptors

Aspirin whose acetyl group forms covalent bond **with cyclo-oxygenase of platelets.**

DNA-alkylating agents in cancer chemotherapy

Electrostatic & Hydrophobic bonds

Electrostatic

Weaker & more common than covalent bonding

Due to linkages between ionic molecules & hydrogen bonds

Force varies from relatively strong linkage to very weak Van der Waal forces

Hydrophobic

Quiet weak, between **highly lipid soluble drugs with the lipids of cell membrane**

Due to interaction of the drug with the internal walls of the receptor pockets

Chirality (stereoisomerism)

What is the role of the shape of the drug molecule?

It permit binding to its receptor site

Drug's shape is complimentary to the receptor site like a key is complimentary to a lock

Shape and charge to 'fit' to only one type of receptors

Chirality (stereoisomerism)

A single chiral molecule --- two enantiomers

> than ½ of all useful drugs are **chiral molecules** ----They exist as **enantiomeric pairs**

Drugs with **two asymmetric centers** have **four diastereomers**

Ephedrine, a sympathomimetic drug

Labetalol, an α & ß receptor blocking drug

Active isomers ---- About 45% of the chiral drugs used clinically are active isomers

Racemic mixture --- The rest are available only as racemic mixtures

More active enantiomer

Inactive

What qualities of the drugs are affected by Chirality (stereoisomerism)?

Potency

One of the enantiomers may be much **more effective** than its mirror image enantiomer, reflecting a **better fit to the receptor site**

Side effects &

Duration of action

Examples -- A single chiral molecule --- two enantiomers

The **levoisomer *s* (-)of adrenaline/epinehrine** is **ten** times more potent than its dextroisomer

S(+) enantiomer of **methacholine**, a parasympathomimetic drug, is over **250 times more potent** than its mirror image enantiomer.

Examples -- A single chiral molecule --- two enantiomers
Carvedilol --
S(-) isomer is a potent ß receptor blocker
R(+) isomer is 100 fold weaker at ß receptor
Equipotent as α receptor blockers
Ketamine
The (+) enantiomer is a potent anesthetic & is less toxic than the (-) enantiomer
Stereoisomerism and receptor binding
Receptor site is like a glove into which the **hand (the drug molecule)** fits to bring its effects
If receptor site is to be like a glove. "left oriented" drug will be more effective in binding to a left-hand receptor than will be its "right oriented" enantiomer

The discovery and development of new drugs
Development and testing process
Drugs are regulated in almost all countries by governmental agencies. In the United States, regulation is by the Food and Drug Administration (FDA)
Safety & Efficacy
Because society expects prescription drugs to be safe and effective, governments regulate the development and marketing of new drugs. In the United States, the FDA proposes and administers these regulations.
Current regulations require evidence of **relative safety** (derived from acute and subacute toxicity testing in animals) and **probable therapeutic action** (from the pharmacologic profile in animals) before **human testing is permitted**.
Some information about the pharmacokinetics of a compound is also required before clinical evaluation is begun.
Chronic toxicity test results are generally not required but must be underway before human studies are started.
Animal Testing
Acute Toxicity
required for all new drugs.
These studies involve administration of single doses of the agent up to the lethal level in at least 2 species (eg, 1 rodent and 1 nonrodent).
Subacute and Chronic Toxicity

required for most agents, especially those intended for chronic use. Tests are usually conducted for a duration in proportion to the time proposed for human application, that is, 2–4 weeks (subacute) or 6–24 months (chronic), in at least **2** species.

Types of Animal Tests
Tests done with animals usually include general screening tests
Pharmacologic profile,
Reproductive effects
Carcinogenicity.

Pharmacologic Profile

Pharmacologic effects of a drug (eg, effects on cardiovascular function, gastrointestinal activity, respiration, renal function, and endocrine function, CNS).
Both graded and quantal dose-response data are gathered.
Reproductive toxicity testing
Need to check either the drug is
teratogenic
mutagenic toxicity.

The FDA uses a 5-level descriptive scale to summarize information regarding the safety of drugs in pregnancy

Teratogenesis
defined as the **induction of developmental defects** in the somatic tissues of the fetus (eg, by exposure of the fetus to a chemical, infection, or radiation).
It is studied by treating pregnant female animals of at **least 2 species** at selected times during early pregnancy when organogenesis is known to take place and by later examining the fetuses or neonates for abnormalities.
Examples of drugs known to have teratogenic effects include thalidomide, isotretinoin, valproic acid, ethanol, glucocorticoids, warfarin, lithium, and androgens.

Mutagenesis

is induction of **changes in the genetic material** of animals of any age and therefore induction of heritable abnormalities.

The **Ames test,** the standard in vitro test for mutagenicity.

- It uses a special strain of salmonella bacteria that naturally depends on specific nutrients in the culture medium.
- Loss of this dependence as a result of exposure to the test drug signals a mutation.
- Many carcinogens (eg, aflatoxin, cancer chemotherapeutic drugs, and other agents that bind to DNA) have mutagenic effects and test positive in the Ames test.

The **dominant lethal test** is an in vivo mutagenicity test carried out in mice.

- Male animals are exposed to the test substance before mating.
- Abnormalities in the results of subsequent mating (eg, loss of embryos, deformed fetuses) signal a mutation in the male's germ cells.

Carcinogenesis

Carcinogenesis is the induction of malignant characteristics in cells.

Carcinogenicity is difficult and expensive to study

Ames test is often used

Agents with known carcinogenic effects include coal tar, aflatoxin, dimethylnitrosamine and other nitrosamines, urethane, vinyl chloride, and the polycyclic aromatic hydrocarbons in tobacco smoke (eg, benzo[*a*]pyrene) and other tobacco products.

Clinical trials

Human testing of new drugs in the United States requires approval

An **Investigational New Drug Exemption application (IND)**, which is submitted by the manufacturer to the FDA

The IND includes all the preclinical data collected up to the time of submission and the detailed proposal for clinical trials.

The major clinical testing process is informally divided into 3 phases that are carried out to provide information for a **New Drug Application (NDA)** .

The NDA constitutes the request for approval of general marketing of the new agent for prescription use and includes all the results of preclinical and clinical testing.

A fourth phase of study (the surveillance phase) follows NDA approval.

Development and testing process

Preclinical study

In vitro studies

Animal testing

Clinical testing

New drug application and registration

Marketing

Post marketing surveillance

Years after filling expires

generics become available

Preclinical testing (1-5 years)

Studies in vitro --- biological products and chemical synthesis

Animal testing

Efficacy, selectivity & mechanism

Pharmacokinetics, pharmacodynamics, & toxic properties

Clinical testing

(phase 1, phase 2, phase 3)

2-10 years (average 5.6 years)

Clinical testing (**phase 1**)

Open trial in research center

By whom? -- Clinical pharmacologist

Why ? ---- Is it safe, pharmacokinetics?

Who? --- Normal **volunteers** (**25-50**)

Volunteer patients --- Cancer , AIDs

special population (renal & hepatic impairment)

Clinical testing (**phase 2**)

Single blind trial (inert placebo, active drug)

By whom? -- Clinical pharmacologist & clinical investigators

Why ?

Does it work in patients

Therapeutic efficacy, dose range, kinetics , metabolism

Who? --- **Selected patients** (100-200)

Clinical testing (**phase 3**)

Double blind & cross over techniques

By whom? -- Clinical investigators

Why ?
Does it work (**efficacy**) & **Safety**
Who?
Large sample of selected patients (may be in thousands) (200-1000)
Post marketing surveillance (**phase 4**)
By whom? -- All physicians
Why ?
Adverse reactions, patterns of drug utilization, additional indications discovered
Who?
Patients given drugs for therapy (2000 ---10,000)

New drug application and registration (NDA)
NDA review - (average 12 months) - NDA approved
Marketing and Post marketing surveillance (Phase 4)
Years (20years) after filing expires (generics available)
An example

The idea

Histamine is potent stimulant of gastric acid secretion
Classic antihistamines did not inhibit this action
There might be a distinct type of histamine receptors

The Clinical Need

Peptic ulcer can be treated by suppressing gastric acid secretion

The Biological Hypothesis

Histamine could be selectively blocked at the receptors that mediate histamine effect on histamine secretion

The Chemical Hypothesis

Classic antihistamines(H_1 blockers) are ineffective
Chemical modification of histamine itself might result in a selective antagonist for the postulated gastric histamine receptors

Development

Pre clinical models and animal testing
A large number of compounds based on histamine structure were synthesized and tested
The first selective H_2 antagonist, burimamide, lacked adequate potency and clinical activity
Burimamide --- metamide --- **cimetidine**
Cimetidine First selective H_2 receptor antagonist in 1974
The research had taken 12 years

In 1992 the sale of H2 receptor antagonist exceeded $ 4 billion

Approaches to develop new drugs

The clinical need

Corticosteroids too toxic for chronic use

Need of anti-inflammatory drugs

The idea -- Identification of a new drug target

Mediators of inflammation especially prostaglandins (PG)

The hypothesis

Inhibitors of prostaglandins

Development

NSAIDs developed (1950-1980)

Aspirin to COX-2 inhibitors

The idea

Willow bark --- used since centuries

Analgesic & antipyretic

Active ingredient --- **Salicin** (1897)

Salicin derivative developed in 1897

Aspirin(acetylsalicylic acid)

Analgesic ,antipyretic + **anti-inflammatory effect**

Adverse effects-- -GI bleed

The clinical need of anti-inflammatory drugs

Corticosteroids too toxic for chronic use

Based on better understandings of mediators of inflammation especially prostaglandins (PG) NSAIDs developed (1950-1980)

More potent than aspirin but had similar toxicities especially of GI adverse effects

The biological hypothesis

Aspirin and NSAIDs inhibit **PG** synthesis

Prostaglandins are mediators of inflammation

Enzyme cyclooxygenase (COX) involved in synthesis of specific PG is increased in inflamed tissue and stimulated by certain cytokines

Isoforms of COX

COX 1 ----- maintain the integrity of lining of the stomach

COX2 --- inducible cox that is upgraded in inflammation

The chemical hypothesis

Cox 2 cloned and expressed in 1991

Screening and rational drug design an inhibitor much more selective for COX2 than for COX 1 was discovered

Celecoxib --- rofecoxib --- valdecoxib

Celcoxib approved in December 1998 for treatment of osteoarthritis and rheumatoid arthritis
Development
NDA for rofecoxib filed in 1998
Clinical trials for clonic polys and Alzheimer's disease started
In1999, the FDA approved the rofecoxib for OA, acute pain, and painful menstruation
Development about 1 year later
First large comparison trial showed a **4 fold risk of heart attack** than non selective Cox inhibitors
In 2002--- label indicating increased CV risk, GI benefit, new use to treat RA
In 2004 second large trial showed twice the risk of hearts an compared to placebo
The manufacturer then voluntarily withdraw rofecoxib
Drug development
Modification of structure of known drug
Aim is to develop a new drugs which are **more active, less toxic or easier to use** than the original drug
Repositioning of a known drug for a new therapeutic use
Amantadine for parkinsonism
Rational drug design

Rational Drug Design
It is the designing of the drug molecule to fit into its receptor on the basis of known **three dimensional structure** of the receptor
Modification of structure of known drug
Homatropine from atropine
Hyoscine butylbromide from hyoscine
Thiazide diuretics from cabonic anhydrase inhibitors
Modification of histamine structure to form H_2 receptor antagonist
Drug act
An act to regulate the import, export, manufacture, storage, distribution and sale of drugs

Why need of drug Act ?
To ensure the availability of standard **quality, safety, efficacy, and Supply of** drugs in hospitals, dispensaries, pharmacies and clinics so that patients get the maximum benefit from the modern drugs.

A basic requirement of any control system is that no medicine may be sold or supplied without prior licensing or registration by government

Health care professionals must understand the implications of this act
&
Should avoid violation of the act during performance of their professional duties.

DRUGS ACT

Drugs Act 1940 and its rules were enforced in India. These rules remained applicable for many years in Pakistan.

In **1972 Generic Drugs Act** was enforced.

According to it the drugs were to be sold under Generic Names and not under Trade Names (Proprietary, Patent Names).

DRUGS ACT

Generic Drugs Act was replaced by ***DRUGS ACT 1976*** and at present this act and rules made there under are enforced in **Pakistan.**

National essential drug list (NEDL)

Essential drug as defined by WHO are those that satisfy the health care need of majority of the population.

They should, therefore, be available at all times in adequate amounts and in appropriate dosage form

NEDL of Pakistan was first prepared in 1994. present list is the 3rd revision containing **425 drugs** of different pharmacological classes

Pakistan National Formulary (PNF)

Federal Ministry of Health, Govt of Pakistan registers drugs (both manufactured in Pakistan or imported from abroad) for marketing in the country.

The registered drugs are published in Pakistan National Formulary (P.N.F.).

Adverse drug reaction monitoring

The form for reporting to
drug controller
Pak. Secretariat, Block C,
Ministry of heath Islamabad

The form

Sr. No

REPORT ON SUSPECTED SERIOUS ADVERSE DRUG REACTION

PARTICULARS OF PATIENT

Name of patient.

Age Weight (kg) Patient address

Sex Male Race

Female

Pregnant Yes No Not applicable

Relevant Medical History

2. ADVERSE EVENT

Reason for reporting

Requires or prolongs hospitalization Life threatening

Death

Permanently disabling or incapacitating Congenital anomaly

Overdose

Other (Please Specify)

3. SUSPECTED DRUG

Name of suspected Drug Generic Name

Name of manufacturer

Date of occurrence Duration of Event

Starting date of Medication

Route of administration

Discontinuation of Drug because of event No Yes

Dated

4. REPORTING DOCTOR'S / PHARMACIST'S / NURSE'S SIGNATURE

Institution

Date

GUIDELINES TO FILL SERIOUS ADVERSE EVENT REPORT FORM

An adverse event is "Serious", if it

- Is life threatening
- Results in permanent disability

- Results in hospitalization
- Is associated with death
- Prolongation of hospitalization
- Causes a birth defect
- Causes malignancy
- Causes a relevant organ toxicity
- Is an overdose resulting in clinically Relevant signs and / or symptoms

An adverse drug event can be a manifestation of various etiologies such as

- Complication of an underlying disease
- Intercurrent disease
- Coincidental accident
- Drug associated effect
- Concomitant medication

Duties of **Drug Inspectors**

To ensure that standard drug are being manufactured and sold in the country.

They take samples of drugs and send to **Drugs Testing Laboratory** for analysis.

If drugs are not of standard quality, they register case against the defaulter in the **Drugs Court** established by the Govt, for this purpose.

If found guilty, the defaulter is punished under the Drgs Act 1976.

Definitions in the drug act

Drug is a substance or a mixture of substances that is manufactured, sold, stored, offered for sale or represented for internal or external use in the treatment, mitigation, prevention or diagnosis of disease in human beings or animals.

Surgical ligatures, sutures, bandages, absorbent cotton, disinfectants, adhesive plasters, gelatin capsules and antiseptic solutions are also included amongst drugs for the purpose of Drugs Act 1976.

Counterfeit Drug

Not genuine; imitating something superior

Make a **copy** of with the intent **to deceive**

A copy that is represented as the original

A drug the label or outer packing of which is an imitation of, or resembles or so nearly resembles as to be calculated to deceive the label or outer packing of a drug of another manufacturer.

Adulterated Drug *– Mixed with impurities*
Corrupt, make impure by adding a foreign or inferior substance; often by **replacing valuable ingredients with inferior ones**
A drug which consists in whole or in part of any filthy, putrid or decomposed substance or any foreign matter

or

which has been manufactured, packed or held under unsanitary condition whereby it may have been contaminated with dirt, filth or any other foreign matter

or

whereby it may have been rendered injurious to health, or it has been mixed with any substance so as to reduce its quality or strength.
Misbranded drug
Branded or labeled falsely and in violation of statutory requirements

A drug which is **not labeled in the prescribed manner** or the label or container of which bears any statement, design or device which **makes any false claim** for the drug.
Spurious Drug
Drug which **does not contain the active ingredient of the drug** which it claims to be or claims to be the product of a manufacturer, place or country whereas it is not truly such product or bears the name of a company but that company is factious or does not exist.
Intended to deceive
Expiry Date of Drug
The date stated on the label of a drug after which the drug is not expected to retain its claimed efficacy, safety, quality, potency or **after which it is not permissible to sell the drug.**

The expiry date will be shorter in case of
Eye drops: can be used for one month after opening the droppers.
Antibiotic syrups & suspensions: generally can be used for one week b y storage in room temperature & for two weeks by storage in refrigera tor.
Ampoules: must be used immediately but the vials (multi-dose) are stable for 24 h in the presence of preservatives.
Nebulizer solution: can be used for one month after opening.
Insulin: once punctured, it must be used within 28 days.

Syrup/Suspension (except antibiotics): can be used for one month aft er opening
Tablets & capsules: remain stable in the package but after removal ex piry date will be changed.