# PAPER III PHARMACOLOGICAL SCREENING METHODS & CLINICAL EVALUATION

**Proposed Hours**

## GOALS:
To understand the process of drug development and estimation of drugs using bioassays. To understand and apply pharmacokinetics to rational drug therapy.

## OBJECTIVES:
Upon completion of the course, the candidate is expected to know

1. The regulations and ethics concerning animal studies and experiments on human beings.
2. Carry out screening of new drugs.
3. Participate in drug development process.
4. Know alternatives to animal screening procedures / techniques
5. To perform Bioassays official in IP/BP/USP.
6. Concepts of kinetics and various pharmacokinetic models

## COURSE DESCRIPTION

### THEORY 50 Hours (2 Hrs/wk)

1. **Drug Design: [6 Hours]**
   a. Drug discovery and development – introduction
   c. Study of laboratory animals including physiological parameters Regulations and ethics requirements. Transgenic animals and other genetically prone animal models (Viz Nude Mice, SH rats and humanized mice).

2. **Preclinical models employed in the screening of new drugs belonging to following categories: [20 Hours]**
   Antipsychotic agent; Antianxiety agents; Nootropic drugs; Antidepressant drugs; Antiparkinsonian agents; Analgesics; Antiepileptics; Antiinflammatory agents; Antiulcer agents; Antianginals and myocardial infarction; Antiarrythmics; Antiatherosclerotic drugs; Antimalarial; Antidiabetics; Antihypertensives; Anticancer.

3. **Modern techniques to elucidate the mechanisms of drug actions: [6 Hours]**
   a. Cell culture and maintenance:
   b. Introduction and applications of Biomarker analysis
   c. Introduction to Translational pharmacology
   d. Alternatives to animal screening procedures, cell-line, patch-clamp technique, in-vitro models.
   e. High throughput screening (HTS): Introduction, Basic principles involved in cell based assays, receptor binding assays and ultra high through put screening.

- **Definition and Scope of Pharmacokinetics.** 1 hour
  Absorption, Distribution, Metabolism, Elimination and transporters

- Individualization: variability, genetics, age and weight, disease, interacting drugs, and monitoring of the same. 1 hour
Pharmacokinetic models: compartmental models, noncompartmental models and physiologic model. Nonlinear pharmacokinetics, multiple dosing and dosage regimen.

**Clinical Research: Introduction and Ethics [3 Hours]**

a. Definition and scope of clinical research. Role of sponsor, study director or principal investigator; Clinical Research Associate in conduct of Clinical Research

b. Study design, ethics in patient selection and preserving their rights. Institutional Ethics Review committee its constituent members and its role in clinical research. Introduction to informed consent and its importance.

**4. Phases of Clinical Trial and Clinical Trial Design [3 Hours]**

a. Calculation of Human Equivalent Dose; Phase 0, Phase I, Phase II, Phase III, Phase IV and Phase V Clinical trial.

b. Randomized Clinical Trial, Uncontrolled Trials, Protocol Development, End points, Patient Selection and blinding, special designs like cross over design, factorial design, Equivalence design, confounding in clinical trials and ways to minimize it, Missing data and its management, occurrence of ADRs, interim monitoring and stopping of trials,

**5. Regulatory Affairs in Clinical Research [5 Hours]**

a. Pharmacovigilance


c. International Guidelines to meet the standards in Clinical Research: ICH guidelines for efficacy testing of drugs: clinical aspects and data management strategies (E1 – E14)

**BOOKS:**

1. Drug Discovery and Evaluation Pharmacological Assay by Vogel H G and Vogel W H (Springer publication)


3. Drug Screening Methods by SK Gupta, Jaypee Brothers, New Delhi.


5. Remington’s Pharmaceutical Sciences 24th edn.


7. Clinical Pharmacology by P N Bennett and Brown


9. Modern Methods of Drug Discovery by Hillisch, A and Hilgenfeld, R

**Reference Books:**


2. Modern drug research- Paths to better and safe drugs (Medicinal Chemistry vol. 9) by Y C Martin, E. Kutter and V. Austel

3. Practical approaches in toxicity studies by Poole and Leslie

4. Pharmacological Experiments in Intact preparations, Edinburgh University Pharmacology staff, Livingstone, (1968)


**Journals:**

1. Indian Journal of Pharmacology [Essential]

3. Drug Metabolism and Pharmacokinetics.

Practicals: [6 hours/week]

3. PA2 values of various antagonists using suitable isolated tissue preparations.
4. In-vitro Absorption study using Inverted rat intestine
5. Exercise on determination of pharmacokinetic parameters using UV/visible spectrophotometer/HPLC
6. Screening of anxiolytic drugs
7. Screening of antidepressant drugs
10. Analgesic by hot plate, tail flick, tail dip, paw pressure test, plantar test and/or writhing methods.
12. Anticonvulsant
13. Pole climbing
14. Actophotometer
15. Exercise on Biostatistics using software
16. Enzyme based in vitro bioassays (5-LO, COX, DPPH, AchE, hyaluronidase inhibition assays)
17. Antioxidant activity of Super oxide dismutase (SOD), Catalase, lipid peroxidation and Reduced glutathione in tissue homogenate