NIPER
RAEBARELI

SYLLABUS

M.S. (Pharm.)
Regulatory Toxicology

M.S. (Pharm.) Regulatory Toxicology

Course No.	Course Name	Credits
Semester-I		
RT-540	Principles and Methods in Toxicology	1
RT-550	Introduction to Regulatory Toxicology	2
*** PC-511	Pathophysiology	1
*** PC-520	General Pharmacology	2
*** PC-530	Experimental Pharmacology	1
**** PE-520	Biopharmaceutics and Pharmacokinetics	2
* GE-510	Biostatistics	2
** GE-520	Fundamentals of Intellectual Property (IP) and Technology Management	1
GE-511	Seminar	1
LG-510	General Lab Experience	3
	Total Credits	**16**
Semester-II		
RT-630	Molecular Toxicology	2
RT-640	Target Organ Toxicology	2
RT-650	Good Laboratory Practice in Regulatory Toxicology	2
RT-660	Bioethics	1
* PC-610	Drug Metabolism	1
** PC-611	Pharmacological Screening and Assays	1
*** PC-650	Clinical Pharmacology and Regulatory Toxicology	2
GE-611	Seminar	1
LS-610	General Lab Experience in the area of Specialization	2
	Total Credits	**14**
Semester-III		
Project (22 weeks)		
TH-598	Synopsis	5
TH-599	Presentation	3
	Total Credits	**8**
Semester-IV		
TH-698	Thesis	9
TH-699	Defence of Thesis	3
	Total Credits	**12**
	Grand Credits (I to IV Semesters)	**50**

Note : * Common in all disciplines
** Common between Pharmaceutics, Pharmacology & Toxicology and Regulatory Toxicology
*** Common between Pharmacology & Toxicology and Regulatory Toxicology
**** Common between Pharmaceutics and Regulatory Toxicology

M.S. (Pharm.) Regulatory Toxicology
SEMESTER - I

RT 540 - Principles and Methods in Toxicology (2 Credits)

1. Introduction to general toxicology.
2. History of toxicology
3. Classification and ramification in toxicology.
4. **Toxicants:** Exposure, exposure characterization
5. **Routes of exposure:** Organism environment interaction
6. Animal and plant toxins.
7. Absorption and distribution of toxicants.
8. Human health risk assessment.
9. **Hazard identification:** Risk assessment
10. Risk prediction and management

Recommended Books:

1. Casarett & Doull's Essentials of Toxicology by Curtis D. Klaassen, John B. Watkins
2. Principles of Toxicology by Karen Stine, Thomas M. Brown
3. Text Book of Pathology by Harsh Mohan

RT 550 - Introduction to Regulatory Toxicology (2 Credits)

1. **Drug discovery and development:** Drug Laws, FDA, OECD, ICH.
2. **Schedule Y:** Design non-clinical toxicity studies and clinical development
3. Clinical risk/benefit analysis.
4. **Drug discovery and registration:** Regulatory affairs, WTO, patent regime, accreditation and harmonization process.
5. **Models and bioassay:** Methods in toxicity testing, dose-response characterization.
6. **Threshold limitations:** Hormesis, lower dose extrapolation.
7. **Animal to human extrapolation:** Flow chart, “Case by Case” basis in non-clinical development and its influences in safety assessment, usefulness and limitations
8. **Regulations of human pharmaceuticals:** Preclinical development.
9. **Environmental impact:** Regulation for biological products.
10. **Influence of new technologies:** Discovery development gap, future of drug safety.

Recommended Books:

1. Regulatory Toxicology by Shayne C. Gad Taylor & Francis
2. Principles and Methods of Toxicology by A. Wallace Hayes

PC 511 - Pathophysiology (1 Credit)

1. Factors influencing the disease conditions such as sex, age, nutritional status, genetic make up etc.

2. Pathogenesis, symptoms and signs, laboratory findings and complications of respiratory, urinary tract, venereal and meningial infections
3. Pathogenesis, symptoms and signs, laboratory findings and complications of Congestive heart failure, hypertension, cardiac arrhythmias
4. Pathogenesis, symptoms and signs, laboratory findings and complications of Ulcer, pancreatitis
5. Pathogenesis, symptoms and signs, laboratory findings and complications of hepatitis and cholecystitis
6. Pathogenesis, symptoms and signs, laboratory findings and complications of Bronchial asthma
7. Pathogenesis, symptoms and signs, laboratory findings and complications of depression, schizophrenia, epilepsy
8. Pathogenesis, symptoms and signs, laboratory findings and complications of Parkinsonism and Alzheimer disease.
9. Pathogenesis, symptoms and signs, laboratory findings and complications of Hypo and hyper thyroidism, diabetes mellitus and other endocrine diseases
10. Pathogenesis, symptoms and signs, laboratory findings and complications of Rheumatoid arthritis, gout and anemia

Recommended Books:

4. Pharmacotherapy: A Pathophysiologic Approach by Dipiro and others
5. The Pharmacological Basis of Therapeutics by Goodman and Gilman's

PC 520 - General Pharmacology (2 Credits)

1. Concept of receptors as a drug target
2. GPCR- Classification, structure, drug receptor interaction, G-protein, receptor characterization, receptor theories, agonist, antagonist
3. Receptor regulation: GPCR desensitization, down regulation, up regulation
4. Regulators of G-protein signaling
5. Ion channels and Ion channel linked receptors and their regulation
6. Nuclear receptors
7. Transmembrane signaling mechanisms
8. Second messenger system
9. Transcription factors: Nrf2 Mechanism of action, pharmacological target and role in different diseases conditions
10. Dose response relationship and different type of antagonism
11. Efficacy and Toxicity evaluation using different experimental models, dose-response analysis, margin of safety in pre-clinical development
12. Chronopharmacology

Recommended Books:

1. The Pharmacological Basis of Therapeutics by Goodman & Gilman
2. Casarett & Doull's Essentials of Toxicology, edited by CD Klassen and JB Watkins
3. Scientific journals in the area of pharmacology(Trends in Pharmacological Sciences, Annual Reviews of Pharmacology and Toxicology, British Journal of Pharmacology, European Journal of Pharmacology, Pharmacology and Therapeutics, Nature Review Drug Discovery, Nature Review Neuroscience, Brain Research)

PC 530 - Experimental Pharmacology (1 Credit)

1. Introduction to pharmacological research
2. Research ethics and publication ethics
3. Common laboratory animals and their physiological parameters, factors affecting the nature and degree of pharmacological responses; Handling and care of different animals; Bleeding and different routes of administration, anaesthetics used in animal research and chemical euthanasia.
4. Animal experimentation: Advantages and disadvantages; Anaesthesia used in laboratory animals, common agents, dose calculations, cannulation methodology, ventilation rate, recording of arterial blood pressure, intestinal motility etc.
5. Conscious animal experimentation, precautions to be taken in behavioural experiments
6. Humanized mouse
7. Imaging techniques in pharmacological research
8. Drug solution preparations: Storage, concentration expression, common solvents, stabilizing agents, storage conditions, reference standards, methods of procurement of reference standards. False positive and false negative response.
9. *In vitro* experimentation: Advantages and disadvantages
10. Animal cell-culture techniques: Aseptic handling, cell counting and cell viability assays. Tissue isolation, tissue fixation, common fixtatives, preparation of single cell suspension.
11. Protein and DNA gel electrophoresis: Western, northern, southern blot hybridization and PCR techniques.
12. Protein purification and identification by two dimensional gel electrophoresis, LCMS-MS, MALDI.

Recommended Books:

1. Drug Discovery and Evaluation: Pharmacological Assays by Vogel& Vogel
2. CPCSEA guidelines (http://cpcsea.nic.in)

PE 520 – Biopharmaceutics and Pharmacokinetics (2 Credit)

1. **Introduction:** Definitions, ADME, concentration time profile, plotting the data, different fluid compartments and blood flow rate compartment models, biological half life, elimination rate constant. Biopharmaceutics and pharmacokinetics in drug research.
2. **GIT Absorption of drugs:** Mechanism, physico-chemical, biological and pharmaceutical factors affecting drug absorption through GIT. Techniques for the GIT absorption assessment.
3. **Drug disposition:** Total body clearance, renal clearance, mechanism of clearance, clearance ratio, factors affecting renal clearance, hepatic clearance, volume of distribution and its significance.
4. **Protein and tissue binding:** Factors affecting protein binding, kinetics of protein binding, determination of rate constant and different plots (direct, scatchard and reciprocal), Implication of protein binding on pharmacokinetic parameters
5. **Bioavailability and bioequivalence:** Definitions, federal requirements, methods of determination of bioavailability using blood and urinary excretion data. Protocol design for bioavailability assessment. Methods for bioequivalence determination.
6. **Pharmacokinetic characterization of drugs:** Pharmacokinetics of drugs following one/ two

compartment open models with first order elimination kinetics as applied to rapid intravenous injection, Intravenous transfusion and oral administration. Determination of absorption rate constant using Wagner-Nelson, Loo Riegelman methods. Flip-flop models, method of residual. Urinary excretion data and its application in pharmacokinetic characterization of drugs. Pharmacokinetics of multiple dosing

7. **Dosage regimen:** Dosage regimen adjustment in patients with renal and hepatic diseases. Drug dosage in elderly, children and obese patients.

8. **Non Linear Pharmacokinetics:** Various causes of non-linearity, Michaelis-Menten kinetics, In-vivo estimation of Km and Vm. Case studies.

9. **Physiologic pharmacokinetics models:** Mean Residence Time; Statistical Moment Theory; Application and limitations of physiologic pharmacokinetic models.

10. **Miscellaneous Topics:** Chronopharmacokinetics, Drug toxicity and forensic pharmacokinetics, kinetics of maternal-fetal drug transfer, pharmacokinetics v/s pharmacological/ clinical response, metabolic kinetics.

Recommended Books:

1. Applied Biopharmaceutics& Pharmacokinetics, by Shargel, L., S. Wu-Pong
2. Biopharmaceutics and Pharmacokinetics: An Introduction by Notari, R. E.
3. Introduction to Biopharmaceutics, by Gibaldi, M.
4. Biopharmaceutics and Relevant Pharmacokinetics, by Wagner, J. G.
5. Textbook of Biopharmaceutics and Clinical Pharmacokinetics by Niazi, S.K.
6. Handbook of Bioequivalence Testing, by Niazi, S. K.
7. Modeling in Biopharmaceutics, Pharmacokinetics, and Pharmacodynamics: Homogeneous and Heterogeneous Approaches, by Macheras, P. and A. Iliadis
8. Comparative Pharmacokinetics: Principles, Techniques and Applications, by Riviere, J. E
9. Foundations of Pharmacokinetics, by Rescigno, A.
10. Clinical Pharmacokinetics and Pharmacodynamics: Concepts and Applications, byRowland, M. and T. N. Tozer

GE 510 - Biostatistics (2 Credits)

1. **Statistics:** Introduction, its role and uses. Collection; Organization; Graphics and pictorial representation of data; Measures of central tendencies and dispersion. Coefficient of variation

2. **Probability:** Basic concepts; Common probability distributions and probability distributions related to normal distribution

3. **Sampling:** Simple random and other sampling procedures. Distribution of sample mean and proportion.

4. **Estimation and Hypothesis Testing:** Point and interval estimation including fiducial limits. Concepts of hypothesis testing and types of errors. Student- t and Chi square tests. Sample size and power

5. **Experimental design and analysis of variance:** Completely randomized, randomized blocks. Latin square and factorial designs. Post- hoc procedures

6. **Correlation and regression:** Graphical presentation of two continuous variables; Pearson's product moment correlation coefficient, its statistical significance. Multiple and partial correlations. Linear regression; Regression line, coefficient of determination, interval estimation and hypothesis testing for population slope. Introduction to multiple linear regression model. Probit and logit transformations

7. **Non-parametric tests:** Sign; Mann-Whitney U; Wilcoxon matched pair; Kruskal wallis and Friedman two way anova tests. Spearman rank correlation

8. **Statistical techniques in pharmaceutics:** Experimental design in clinical trials; Parallel and crossover designs. Statistical test for bioequivalence. Dose response studies; Statistical quality control

Recommended Books:

1. Fundamentals of Biostatistics by Bernard Rosner
2. Pharmaceutical Statistics: Practical and Clinical Applications by Bolton and Bon
3. Statistical Misconceptions by Huck

GE 520 - Fundamentals of Intellectual Property (IP) and Technology Management (1 Credit)

1. **Intellectual property:** Concepts and fundamentals; Concepts regarding intellectual property (IP), intellectual property protection (IPP) and intellectual property rights (IPR); Economic importance, mechanisms for protection of intellectual property-patents, copyrights, trademark; Factors effecting choice of IP protection; Penalities for violation; Role of IP in pharmaceutical industry; Global ramifications and financial implications.

2. **Trade related aspects of intellectual property rights:** Intellectual property and international trade; Concept behind WTO (World Trade Organisation), WIPO (World Intellectual Property Organisation) GATT (General Agreement on Tariff and Trade), TRIPs (Trade Related Intellectual Property Rights), TRIMS (Trade Related Investment Measures) and GATS (General Agreement on Trade in Services); Protection of plant and animal genetic resources; Biological materials; Gene patenting; Biotechnology / drug related IPR issues; Status in India and other developing countries; Case studies and examples; TRIPS issues on herbal drugs.

3. **Nuts and bolts of patenting, copyright and trademark protection criteria for patentability, types of patents; Indian Patent Act, 1970; WTO and modifications under TRIPS:** Filing of a patent application; Precautions before patenting-disclosures / non-disclosures, publication-article / thesis; Prior art search-published patents, internet search patent sites, specialized services-search requests, costs; Patent application-forms and guidelines, fee structure, time frames, jurisdiction aspects; Types of patent applications-provisional, non provisional, PCT and convention patent applications; International patenting-requirement procedures and costs; Financial assistance for patenting- introduction to schemes by NRDC and TIFAC; Publication of patents-gazette of India, status in Europe and US; Patent annuity; Patent attomeys technical aspects, criteria for selection, addresses, fee, rights and responsibilities of a patentee; Practical aspects regarding maintaining of a PATENT FILE; Patent infrigment- meaning, scope, litigation, case studies and examples; Patenting by research students, lecturers and scientists-University / organisational rules in India and abroad; Thesis research paper publication, credit sharing by workers, financial incentives; Useful information sources for patents related information-internet sites, brouchers, periodicals, CD roms; Significance of copyright protection for researchers; Indian Copyright Law and digital technologies-Beme convention, WIPO copyright treaty (WCT), WIPO performance and Phonogram Treaty (WPPT); Protection for computer data bases, multi media works; Trademarks legislation and registration system in India-an introduction, meaning of trademark criteria for eligibility; filling application for trademark registration; Trade secrets-scope modalities and protection; Case studies-drug related patents infringements.

4. **Technology development / transfer / commercialisation related aspects:** Technology development-meaning; Drug related technology development; Toxicological studies, bioequivalence (BU), clinical trials-phase-I, phase-II and phase-III; Approved bodies and agencies; Scale-up, semi-commercialisation and commercialisation-practical aspects and problems; Significance of transfer of technology (TOT), bottlenecks; Managing technology transfer-guidelines for research students, scientists and related personal; TOT agencies in India-APCTD, NRDC, TIFAC, BCIL, TBSE/SIDBI; TOT related documentation-confidentiality agreements, licensing, MOUs, legal issues; Compulsory licensing excess to medicine issues; DOHA declaration, POST WTO product patent regime from 2005; Challenges for Indian pharmaceutical industry in the context of globalisation of IP; Drug registration and licensing issues-national and global; Drug master file submissions, SOPS; Related registration and marketing issues; Case studies-antiretroviral drugs and others

5. **Funding sources for commercialization of technology:** Preparation of a project report, financial appraisal, business models; GOI schemes and incentives; NRDC, TePP, HGT, TDB schemes. PATSER; Venture capitalists, banks. Incubator concept-Case studies with respect to

IIT, CCMB, IMTECH, and NIPER. Documentation and related aspects.

6. **Ethics and values in IP:** IP and ethics-positive and negative aspects of IPP; Societal responsibility; Avoiding unethical practices; Echo-responsibility-economic, social and environmental benifits of modern biotechnology; Voluntary adoption of pollution control strategies

Recommended Books:

1. Law Relating to Intellectual Property by B.L.Wadhera
2. IPR Handbook for Pharma Students and Researchers by P.Bansal
3. The Patents Act, 1970 (Bare Act with Short Notes) (New Delhi: Universal Law Publishing Company Pvt. Ltd. 2012)
4. Patent Agent Examination by Sheetal Chopra and Akash Taneja
5. Making Innovation Happen- A simple and Effective Guide to Turning Ideas into Reality by Michael Morgan
6. Making Breakthrough Innovation Happen by Porus Munshi
7. Innovation X- Why a Company's Toughest Problems are its Greatest Advantage by Adam Richardson
8. Legal Drafting for the Layman by Nabhi Kumar Jain
9. How to Write and Publish a Scientific Paper by Rober A Day
10. Concise Law Dictionary-with Legal Maxims, Latin Terms and Words and Phrases by Justice Y.V.Chandrachud
11. Biomedical Research- From Ideation to Publication by G.Jagadeesh and others

GE 511 - Seminar (1 Credit)

1. Introduction, information retrieval systems
2. Writing term papers and reports
3. Organization of scientific material, thesis, dissertation and references
4. Reading research papers
5. Skill in oral presentation

Each student has to present a seminar before end of the semester

LG 510 - General Laboratory Experience -15 hours / week (3 Credits)

1. **Computer and application in pharmaceutical sciences (100 hours):** Introduction to computers, basic unit and functions, H/W and S/W, operating systems, word processing, spread sheet, graphic programs, dbase, windows, statistical S/W programs and packages.

   Steps involved in S/W development, computer languages with emphasis to FORTRAN language and programming, hands on experience in pharmaceutical software systems.

   Use of computers in information retrieval systems

2. **Pharmacology (25 hours):** Animal handling, route of administration of drugs, dose response relationship, analgesic activity of a compound, estimation of protein and haematological parameters.

3. **Specialization (145 hours):** Experiment protocol, quarantine procedures; Animal health checkups, acclimatization, grouping, animal marking; Cage cards, dose calculation for mice and rats; Common solvents, uses, storage conditions, dosing procedures (oral, intraperitoneal); Common toxic symptoms- definitions and observation, feed intake measurements, water intake measurements, urine output, anesthesia and gross necropsy;

   Blood removal from mice and rats and anticoagulants. Separation and isolation of plasma, case of hemolysis sample. Body weight, organ weight, body to organ ratio calculation, different target organs isolation, fixative, preservations, autolysis, raw data collection, computation, statistics and report preparation

M.S. (Pharm.) Regulatory Toxicology
SEMESTER - II

RT 630 - Molecular Toxicology (2 Credits)

1. **Cell signaling and receptor mediated toxicity- Ion channels:** Receptors linked to protein kinases and phosphatases, intracellular receptors
2. **Second messengers:** Signaling to the nucleus, general overview of mechanisms of cell death.
3. **Calcium- mediated toxicity:** Excitory amino acid toxicity. No toxicity
4. **Cytokines toxicity:** Steroid hormone induced toxicity
5. **Signaling and apoptosis:** Methods of studying receptors
6. **Methods for studying cell signaling:** Mechanism of chemical toxicity
7. **Oxidative stress:** Apoptosis, necrosis, comparison and significance in toxicity evaluation
8. **Toxicogeneomics and microarray:** Expression profiling in prediction of toxicology, principles problems and prospects. Early predictions, impact to reduce attrition in drug development
9. **New assays:** New procedures of evaluation, phototoxicity, coment assay, modified *Salmonella assay*, transgenic bioassays, neonatal bioassays, validation procedures, uses and limitations
10. **In- vitro bioassays:** Predictive and mechanistic toxicology, different cell lines their use and limitations

Recommended Books:

1. Molecular Toxicology by P. David Josephy
2. Advances in Molecular Toxicology by James C. Fishbein
3. Cellular and Molecular Toxicology and In Vitro Toxicology by Daniel Acosta
4. Lehninger Principles of Biochemistry (5th Edition) by M.M. Cox and DL Nelson

RT 640 - Target Organ Toxicology (2 Credits)

1. Haematotoxicity: Blood pictures, cell types and pathology
2. Hepatotoxicity: Liver structure, functions and pathology
3. Nephrotoxicity: Kidney morphology and pathology
4. Local toxicity: Skin morphology and pathology
5. Cardiotoxicity: Cardiovascular structure and pathology
6. Neurotoxicity: Structure and pathology. Bone marrow toxicity
7. Targets of toxic drugs: Toxicity of chemotherapeutic drugs, antibiotics, antiviral agents
8. Toxicity of drugs used for chronic treatment: Drug pollutant interactions
9. Endocrine disruptors: Emphasis on neurotoxic, genotoxic and carcinogenic agents.
10. Historical control data: Importance in generation of quality data, back ground lesions, Use of suitable animal models in toxicity evaluation

Recommended Books:

1. Robins Basic Pathology, by Saunders, Elsevier
2. Text Book of Pathology, by Harish Mohan, Jaypee

RT 650 - Good Laboratory Practice in Regulatory Toxicology (2 Credits)

1. Good Laboratory Practices (GLP).
2. Quality control and Quality Assurance
3. SOP writing and implementation: GLP Establishment
4. Study plans: Study protocols
5. Master schedule: Responsibility of study directors
6. Multisite management and principles investigators responsibility
7. Reporting of study results.
8. Storage and retention of records and materials.
9. GLP audits and inspections.
10. Cost benefit comparisons, in regulatory set ups

Recommended Books:

1. Good Laboratory Practice, 2nd Edition, by Jurg P Seiler, Springer
2. WHO/TDR Manual for Good Laboratory Practice, WHO/TDR, Geneva, Switzerland

RT 660 - Bioethics (1 Credit)

1. Ethics moral and laws relative to animals.
2. Trade regulations.
3. Market requirement.
4. Import and export rules.
5. Social pressure and friendly use of animals in higher research.
6. Approval process for use of animals in experiments
7. Precautions in biological experiments.
8. Labeling: Identification, cage cards.
9. Handling of experimental animals.
10. Disposal of dead animals after experiments.

Recommended Books:

1. Animal bioethics Principles and Teaching Methods, edited by M. Marie, S. Edwards, G. Gandini, M.
2. Reiss and E. von Borell
3. The Palgrave Macmillan Series on Animal Ethics, edited by Andrew Linzey and Priscilla Cohn
4. Nonhuman Primates in Biomedical Research, Diseases by Taylor Bennett, Christian R. Abee, Roy Henrickson

PC 610 - Drug Metabolism (1 Credit)

1. Biotransformation of drugs.
2. Enzymes responsible for bio-transformations, microsomal a non-microsomal mechanisms
3. Factors influencing enzyme induction and inhibition.

4. Factors effecting drug metabolism.
5. Drug metabolism in fetus and new born.
6. Models of study drug metabolism.
7. Dose-effect relationships.
8. Excretion of drugs, biliary and fecal excretion.
9. Adverse drug reactions and drug interactions; Toxic reactions, allergic reactions, indiosyncracy.
10. Acute poisoning and its treatment

Recommended Books:

1. Introduction to Drug Metabolism, by G. Gordon Gibson and Paul Skett
2. Drug Metabolism Handbook Concepts and Applications Edited by Ala F. Nassar, Wiley

PC 611 - Pharmacological Screening and Assays (1 Credit)

1. Role of pharmacology in drug discovery
2. General principles of pharmacological screening.
3. Animal ethics, regulations for conducting animal experimentation.
4. 3 R's concept, alternatives to animal experimentations, Organs-on-chips
5. Pharmacological screening models.
6. Correlations between various animal models and human situations.
7. Correlation between in-vitro and in-vivo screens
8. Cell- based assay, CaCo-2 cell permeability assay. Single cell gel electrophoresis assay (COMET) assay
9. Zebrafish model to screen pharmaceutical molecules
10. Biochemical assays
11. Introduction to cell culture, role of genomic and proteomic techniques in the process of target identification in drug discovery, MALdiTof., microarray
12. High throughput screening and high content screening, transgenic animal model for drug screening
13. Specific use of reference drugs
14. Interpretation of results
15. Pharmacogenomics and Personal medicine

Recommended Books/ Journals:

1. Drug Discovery and Evaluation: Pharmacological Assays by Vogel & Vogel
2. CPCSEA guidelines (http://cpcsea.nic.in)
3. Scientific journals in the area of pharmacology

PC 650 - Clinical Pharmacology and Regulatory Toxicology (2 Credits)

1. Introduction to clinical pharmacology
2. Investigational new drug (IND) application, clinical trials, new drug application (NDA) requirements; Regulatory agencies

3. Pharmacovigilance,
4. GCP Guidelines and GLP Guidelines
5. Individualization of drug therapy: Personalized medicine
6. Preclinical testing strategy; Vis-à-vis envisaged clinical studies; Experimental clarification of possible human risk; Technical details of experiments; Flow chart for development of preclinical testing.
7. Single dose and repeat dose toxicity studies: Factors influencing such studies such as species, sex, route, dose level; Data evaluation and regulatory requirements.
8. Reproductive toxicology assessment of male reproductive toxicity: Spermatogenesis; Risk assessment in male reproductive toxicity; Female reproductive toxicology; Oocyte toxicity.
9. Mutagenicity: Mechanisms of mutagenesis, germ cell mutations, somatic cell mutation; Tests systems in vitro, test for gene mutation in bacteria, chromosome damage, in vivo micronucleus tests in rodent, metaphase analysis.
10. Carcinogenicity: Principles of carcinogenicity, dose-setting for carcinogenesis bio assay, transplacental carcinogenesis; Cocarcinogenisis/tumor promotion.
11. Toxicokinetics, animals and dose groups: Exposure measurement; determination of metabolities complicating factors in exposure interpretation, analytical method, good laboratory practices; Stereiosomerism vis-à-vis regulatory requirements; Single enantiomers; Racemate enantiomer switch; Regulatory requirements.
12. Preclinical toxicological requirements for biological and biotechnological products: Safety analysis; problems specific to recombinant products secondary pharmacology.
13. Safety Pharmacology - ICH S7 and S7B guidelines
14. Safety pharmacological studies for pharmaceuticals
15. Safety pharmacological studies for biological products

Recommended Books/ Journals:

1. Clinical Pharmacology by Lawrence
2. Basic and Clinical Pharmacology by Katzung
3. ICH Guidelines
4. Schedule Y
5. OECD Guidelines
6. US FDA Guidelines

GE 611 - Seminar (1 Credit)

Students are required to submit written record and present deta.ls of the project to be pursued in semester-Ill & IV This should include the purpose and basis of the project, stating aims, objectives and probable outcomes, be able to supplement these with necessary information, literature review towards it and process for the project itself

LS 610 - General Laboratory Experience 10 hours/week (2 Credits)

1. Route of administration (ip, iv, po)
2. Blood collection and plasma separation.
3. Blood cell counting (manual and 5 part automation).
4. Tissue isolation and fixation.
5. Tissue processing and histological slide preparation.

6. Blood smear and histological slide staining (manual and automation).
7. Aseptic techniques.
8. Cell culture techniques.
9. Cytotoxicity determination by MTT, LDH and neutral red uptake assay.
10. Use of statistics.
11. Data collection, interpretation and calculations. Health checkups, acclimatization, grouping, animal marking; Cage cards, dose calculation for mice and rats; Common solvents, uses, storage conditions, dosing procedures (oral, intraperitoneal); Common toxic symptoms-definitions and observation, feed intake measurements, water intake measurements, urine output, anesthesia and gross necropsy; Blood removal from mice and rats and anticoagulants. Separation and isolation of plasma, case of hemolysis sample.

    Body weight, organ weight, body to organ ratio calculation, different target organs isolation,

    fixative, preservations, autolysis, raw data collection, computation, statistics and report preparation.