M. PHARM. – CLINICAL RESEARCH
COURSE STRUCTURE (w. e. f. 2011-12)

I SEMESTER					
Course No.	**Title**	**L(h)**	**T(h)**	**P(h)**	**C**
	THEORY				
MPS1101	Advanced Instrumental Analysis (AIA)	3	1	0	4
MPS1141	Quality Assurance & Quality Control	3	0	0	3
MPS1143	Good Clinical and Laboratory Practices	3	0	0	3
	LAB				
MPS1112	Modern Analytical Techniques Lab	0	0	3	2
MPS1132	Preclinical Studies Lab	0	0	3	2
	BREADTH				
MMA1101	Applied Science: Biostatistics	3	0	0	3
	Breadth Paper	3	0	0	3
	Total	**15**	**1**	**6**	**20**
	Total Hours	**22**			
II SEMESTER					
	THEORY				
MPS2131	Clinical Pharmacology & Pharmacotherapeutics	3	0	0	3
MPS2141	Clinical Research – Ethics and Design	3	0	0	3
MPS2143	*Clinical Data Management	3	0	0	3
	ELECTIVE(ANY ONE)				
MPS2101 **MCR3101** **MPSE111**	Biopharmaceutics & Pharmacokinetics Pharmacovigilance Drug Regulatory Affairs	3	0	0	3
	LAB				
MPS2142	Quality Control Lab	0	0	2	2
MPS2144	Biochemical Analysis Lab.	0	0	2	2
MPS2146	*CDM Lab	0	0	2	2
MPS2148	*SAS Lab	0	0	2	2
	Total	**12**	**0**	**12**	**20**
	Total Hours	**24**			
III SEMESTER					
MPS3141	THESIS	-	-	-	**15**
IV SEMESTER					
MPS4141	THESIS	-	-	-	**20**

Total Credit - 75

Note:
L: Lecture; T: Tutorial; P: Practical; C: Credit
MPS: M. Pharm. Pharmaceutical Sciences Core
MPSE: M. Pharm. Pharmaceutical Sciences ELECTIVE
MMA: Mathematics
MCR: M.S. Pharmaceutical Sciences Core
* Will be offered in 3rd semester at LCRA, Bangalore

M. PHARM I SEMESTER
MPS1101: ADVANCED INSTRUMENTAL ANALYSIS (AIA) (4 CREDITS)

1. Analytical Application of Absorption Spectra: 3h
   Absorptiometric assay of Organic Compounds, Structural Analysis.
2. Infrared Spectrophotometry: 6h
   Qualitative uses; Interpretation of I.R. Spectra, Quantitative analysis**.**
3. NMR-Spectroscopy: 8h
   The NMR-Signal, Instrumentation practical consideration, chemical shift, spin-spin coupling, Structure elucidation, investigation of dynamic properties of molecules, quantitative analysis.
4. Mass Spectrometry: 8h
   Theory instrumentation, practical consideration, structure elucidation, detection of impurities, quantitative analysis, application to determination of structure, the gas chromatograph mass spectrometer combination.
5. Optical Rotatory Dispersion: 3h
   Terminology Plain Curves, Rotatory dispersion of ketones, The Axial Haloketone Rule, Octant Rule.
6. Recent trends in chromatography with reference to analysis of drugs and related substances: HPLC, UPLC, HPTLC , GC and hyphenated techniques(LC-MS/ LC-MS/MS).
   8h
7. Theory, Instrumentation and Applications of: 8h
   Thermogravimetric Analysis (TGA), Differential thermal analysis (DTA), Differential Scanning Calorimeter (DSC), X ray Diffraction(XRD).

BOOKS RECOMMENDED:

1. Practical Pharmaceutical Chemistry (part II) by Beckett and Stenlake.
2. Optical Rotatory Dispersion by C. D.jerassi (For ORD).
3. Indian Pharmaceutical (Biological & Microbiological Assay).
4. British Pharmaceutical (Biological & Microbiological Assay).
5. UV and Visible Spectroscopy, Chemical Application-C.N. R. Rao.
6. Spectrometric identification of organic compound- Silverstein.
7. Chemical application of IR spectroscopy – C.N.R. Rao.
8. Physical Methods of Organic Chemistry- Weissberger.
9. Interpretation of Mass Spectra of organic compounds-B. Kienicz, C. Djerassi.
10. Application of NMR Spectra to Organic Chemistry-Jackmann.
11. Instrumental Methods of Analysis- Willard.
12. Applications of Absorption spectroscopy of organic compounds – John R. Dyer.
13. Pharmaceutical Experiments on isolated preparations by the staff of the Department of Pharmacology, University of Edinburg.
14. Pharmacological Techniques in Drug evaluation, Vol. 1&2 by Peter E. Siegler, J.H. Meyer.
15. Lewis Pharmacology- James Crossland.
16. Fundamental of Experimental Pharmacology- M.N. Ghosh.
17. Indian Pharmacopoeia.
18. British Pharmacopoeia.
19. United States Pharmacopoeia .
20. Assay of Vitamins by Haskmi

MPS1141: QUALITY ASSURANCE & QUALITY CONTROL (3 CREDITS)

I. Basic concept of Quality Control & Quality Assurance, Total Quality Management, Philosophy of GMP, cGMP, GLP, ISO, Introduction to ICH guidelines. 4h

II. In Process quality controls on various dosage forms-sterile and non sterile, SOPs for various operations. Quality Assurance guidelines for human blood products and large volume parenterals. 7h

III. Quality Control Laboratory - Responsibilities and laboratory practices, Routine controls on instruments, standard test procedure sampling plans etc. Quality control documentation and audits of quality control facilities. 7h

IV. Introduction to validation – Equipment validation, Calibration of equipments, Method validation, Personnel & Process validation, Asceptic validation, Validation of water and air handling systems. 7h

V. Regulatory Audits – QA in Bioanalytical Laboratory, Medical diagnostic laboratory and Clinical Departments. 6h

VI. Quality assurance in Regulatory Affairs and compliance: Queries and Query resolution, fraud and misconduct, auditing and inspection. 6h

VII. Development, Submission and storage of Quality assurance reports. 3h

Books Recommended:

1. A Practical guide to Quality management in Clinical Trial research, Graham D. Ogg, CRC Taylor and Francis.
2. Clinical audit in Pharmaceutical Development, Michael R.hamrell, Informa Health Care.
3. Validation and Qualification in Analytical Laboratories, Ludwig Huber, Marcel Dekker series.
4. Quality Assurance in Pharmaceuticals, OPPI Publication.
5. Pharmaceutical Process Validation by Berry IR and Nash RA (Eds.) Marcel Dekker Inc., NY.
6. How to Practice GMPs 2nd Edn. By Sharma P.P., Vandana Publishing, New Delhi
7. A Guide to Total Quality Management – Kaushik Maitra and Sedhan K. Ghosh

MPS1143: GOOD CLINICAL & LABORATORY PRACTICES (3 CREDITS)

1. Introduction, Overview of ICH - GCP, Roles & Responsibilities of sponsor, Investigator, Institutional Review Board/Independent Ethics Committee (IRB/IEC),Investigator's Brochure, Essential documents. DSCO, GCP – salient Features,Orphan Drugs – classification, development, marketing, distribution and Orphan Drug Act 1983
   4h

2. **Investigator's Brochure: -** 6h
   - Introduction, General Considerations, Contents of the Investigator's Brochure – Table of contents, Summary, Introduction, Physical, Chemical & Pharmaceutical properties & Formulation, Nonclinical studies, Effects in Humans, Summary of Data & Guidance for the Investigator.
   - Qualifications & agreements, Adequate Resources, Medical Care of Trial Subjects, Communication with IRB/IEB, Compliance with Protocol, Investigation Product, Randomization Procedures and Unblinding, Informed Consent of Trial Subjects, Records & Reports, Progress Reports, Safety Reporting, Premature Termination or Suspension of a Trial, Final Report by Investigator

3. **Sponsor: -** 5h
   QA & QC, CRO, Medical Expertise, Trial Design, Trial Management, Data Handling & Records Keeping, Investigators Selection, Allocation of duties & Functions, Compensation of Subjects & Investigators, Financing, Notification/Submission to Regulatory authority, Confirmation of Investigational Products, Manufacturing, Packaging, Labeling and Coding Investigational Products, Supplying & Handling Investigation Product, Record Access, Safety Information, Adverse Drug Reaction Reporting, Monitoring, Audit, Noncompliance, Premature Termination or Suspension of a Trial, Clinical Trial/Study Reports, Multicentre Trials.

4. **Clinical Trial Protocol Amendment:** 10h
   General Information, Background Information, Trial Objective & Purpose, Trial Design, Selection & Withdrawal of Subjects, Treatment of Subject, Assessment of Efficacy, Assessment of Safety, Statistics, Direct Access to Source Data/Documents, Quality Control & Quality Assurance procedures, Ethics, Data Handling & Record Keeping, Financing & Insurance, Publication Policy Supplements.
5. **Essential Documents for the Conduct of a Clinical Trial** 3h
   Introduction, Before the Clinical Phase of the Trial Commences, During the Clinical Conduct of the Trial, After Completion or Termination of the Trial.

6. **Definition, Overview, Application and Fundamentals of GLP**: 6h

   Resources : Facilities – Infrastructure & Personnel, Rules : Introduction, Protocols & SOPs
   Characterization : Test Item & Test system, Documentation : Experiments, Observations, Records & recording, Quality Assurance : Protocol review, SOP review, Planning Audits & Inspections, Quality Assurance Statement, QAU inspection of suppliers & contractors, Distribution & archiving of QAU files & reports along with OECD guidelines

7. **Implementation of GLP :** 6h

   Introduction , Implementation as a project (Development of SOPs, Simple protocols, Evaluation etc.),Stepwise implementation of GLP requirement

Books Recommended:

1. Principal and Practice of Pharmaceutical Medicine edited by Andrew J. Fletcher, Lionel D. Edwards, Anthony W.Fox Peter Stonier, published by John Wiley and Sons Ltd.
2. Clinical Pharmacotherapeutics –ed., K. Kohli, Elsevier Publication.
3. Statistical Methods for Clinical Trials, by Marc X Norleans , Marcel and Dekker, Inc., New York 2001.
4. Good Laboratory Practice Regulations by Weinberg, Marcel Dekker Inc., NY.
5. Good Laboratory Practice by Sharma P.P., Vandana Publishing, New Delhi.

MPS1112 MODERN ANALYTICAL TECHNIQUES LAB (2 Credits)

1. Determination of λmax. Of given sample using Spectrocolorimeter and validity of Lambert-Beer's Law.
2. Assay of Paracetamol Tablets using UV-Spectrophotometer.
3. Assay of Quinine Sulphate using UV-Spectrophotometer.
4. Assay of Nimesulide Tablets using UV-Spectrophotometer.
5. Assay of Riboflavin Tablets using Fluorescence Spectrophotometer.
6. Assay of Quinine Sulphate tablets using Fluorescence Spectrophotometer.
7. Determination of of Na^+ & K^+ using Flame Photometer.
8. Determination of Dextrose in Dextrose Injection using Polarimeter.
9. Determination of α-Amino Acid using pH-Meter.
10. Assay of Paracetamol in the sample using HPLC.
11. Demonstration of functional groups of the given samples I.R.Spectrophotometer.
12. Assay of Paracetamol in the sample using HPTLC.
13. Labs related to Clinical Research

MPS1132: PRECLINICAL STUDIES LAB (2 Credits)

1. Experimental Techniques to evaluate the various classes of drugs (in vivo studies) (at least 10-12 experiments).

   A. Drugs acting on GIT: - General screening methods of ulcer activity, intestinal motility, & anti-diarrhoeal
   B. Experiments on toxicology: - Oral, Parentral & skin acute toxicity test.
   C. Experiments on Analgesic & Antipyretic drugs.

Reference:

1. Biological standardization by J.H. Burn, D.J. Finney & L.G. Goodwin.
2. I.P. & B.P.
3. Screening Methods in Pharmacology – R.A. Turner.
4. Evaluation of drug activities by Laurance & Bacherce.
5. Methods in Pharmacology by Arnold Schwartz.
6. Selected topics on Experiment Pharmacology by Issha G. Kamat, Dadkar, N.K. & Seth, UK.
7. Fundamental of Experiment Pharmacology – M.N. Gl.
8. Pharmacological Experiment on intact preparation by Churchill Livingstone
9. Drug Discovery & Evaluation by Vogel HG.
10. Animal Model in Toxicology by Shayne Cox Gad & Christopher P, Chengelis.
11. Principles & Methods of Toxicology by Hays.
12. CRC Handbook of Toxicology by Derelako & Hollinger.

M. PHARM II SEMESTER
MPS2131: CLINICAL PHARMACOLOGY & PHARMACOTHERAPEUTICS
(3 CREDITS)

Pathophysiology & applied Pharmacotherapeutic management of diseases associated with following system / diseases.

1. Nervous System 6 h

Pain and Pain Management, Pathophysiology to inflammation and repair, Pain pathways, Anaesthesia and Neuromuscular block
Epilepsy, Parkinsonism, schizophrenia, depression, migraine, Alzheimer's disease

2. Cardiovascular System 9h

Hypertension, Congestive cardiac failure, Ischemic heart disease (Angina, Myocardial infarction), Arrhythmias, Hyperlipidemias, atherosclerosis, Endocarditis, Thromboembolic disorder.
Haemostasis, Anaemia, Blood Substituents, Drug induced haematological disorders.

3. Respiratory System 4 h

Pulmonary function tests, bronchial asthma, Chronic obstructive airways diseases, Drug induced pulmonary diseases.

4. Renal & Endocrine System 11 h

Diuretic therapy, Potasium depletion, Hyperkalaemia, Acute Renal failure, Chronic renal failure, Drug induced renal diseases.
Adrenal corticoids, antagonists, Thyroid hormones & antithyroid drugs, Diabetes Mellitus, thyroid and parathyroid diseases, Hormone replacement therapy,

5. Gastrointestinal System 4 h

Ulcer diseases, Inflammatory Bowel Diseases, Hepatitis, cirrhosis, Jaundice, Diarrhoeas & Constipation,

6. Bone and joint disorders 4 h

Osteoporosis, rheumatoid arthritis, Osteoarthritis, gout, Paget's diseases of bones. Geriatric, Paediatric & Perinatal Pharmacology.

7. Neoplastic disorders & infections 6h

Acute leukemias, Hodgkins disease and carcinoma of breast etc.
Various infectious diseases including Tuberculosis, urinary tract infections, enteric infections, upper respiratory tract infections, sexually transmitted diseases and AIDS.

References:

1. Clinical Pharmacology by P.N. Bennet & M. J. Brown eds. 9th edn., Churchill Livingstone.
2. Clinical Pharmacy and Therapeutics – Eric Herfindal, Williams and Wilkins Publication.
3. Pathologic basis of diseases – Robins SL, W.B. Sunders Publicaton.
4. Davidson's Principle and Practice of Medicine, Eds. Christopher R. W., Edwards & Ian A.D. Boucher ELBS with Cdnorchill Living stone. Edinburgh. Latest Edition.
5. Harrisons Principles of Internal Medicine. Medical Toxicology (Ellen Horns).
6. Oxford Text Book of Clinical Pharmacology and Drug Therapy, 3rd edition, Graham-Smith D. and Aronson J., Oxford University Press
7. Principles of Pharmacology, the Pathophysiologic Basis of Drug Therapy,Lippincott, Williams & Wilkins.
8. CRC desk reference of Clinical Pharmacology, Manuchair Ebadi.
9. Oxford Text Book of Pharmaceutical Medicine, 4th edition, John P. Griffin, John O'Grady.
10. Oxford Text Book of Medicine, 4th edition, David A. Warrell, Timothy M. Cox, John D. Firth.
11. Pathology & Therapeutics for Pharmacists. Russel. J. Greene and Normal F.Harris. Chapman & Hall, London/ Glasgow/ Madras.
12. Text Book of Therapeutics: Drug and Disease Management. 7th Edition. Editors: Eric T. Herfindal and Dick R. Gourley, Williams and Wilkins, 2000

MPS2141: CLINICAL RESEARCH – ETHICS & DESIGN (3 CREDITS)

1. Clinical Research – Introduction, History, Present & Future Scenario 2h
2. Drug Development – Discovery, Screening, Formulation, Preclinical, Various Phases (Phase I to Phase IV) of Clinical Study, Clinical & Product Registration 3h
3. BA/BE Studies 1h
4. Investigational New Drug & New Drug Application 1h
5. Regulations – Schedule Y, 21CFR part 11, 50, 54, 56, 310, 312, Drug Registration: Introduction, U.S regulation, Japan regulation, U.K regulation, Indian regulation, Ethnic Insures in drug Registration. 4h
6. Study Participants – Sponsor, Investigator, Volunteer, Contract Research Organization, Data Safety & Monitoring Board 3h
7. Ethics – Principles & Practices --- History, Ethical Principles, Clinical Trial Regulations, Declaration of Helsinki, Ethics Committee, Informed Consent, Investigator's Responsibilities, Vulnerable populations 4h
8. Study Setup – Feasibility assessment, Site selection, Budget proposal 2h
9. Study Monitoring – Monitoring Responsibilities: Type of monitoring visits, Site Initiation, Interim Monitoring, Site close out, monitoring activities, Monitoring methods, Problem solving, Writing monitoring reports 8h
10. Investigational Product Management – Accountability, Distribution 2h
11. Study Design & Planning – Design, Study Protocol, Case Report Form, Quality of Life, Study Plan, Study Flow Chart, Investigator Selection, Clinical Trial Application 5h
12. Organization – Contracts & Agreements, Liability & Insurance, Financial Disclosure, Clinical Trial Committees, Logistics & Clinical Laboratory 3h
13. Study Conduct – Essential Documents, Subject Recruitment, Randomization & Blinding, Investigational Product Management, Clinical Trial Supplies 3h
14. Safety Reporting – Adverse Events, Serious Adverse Events, Adverse Drug Reactions, Patient Care in Clinical Research, Pharmacovigilance 2h
15. Study Report – Interpretation, Report & Retention of data/report 2h

Books Recommended

1. Principal and practice of Pharmaceutical Medicine edited by Andrew j Fleteher. Lionel D Edwards, Anthony W Fox. Peter Stonier Published by John Wiley & sons Ltd.
2. Clinical Pharmacotherapeutics- edited by Kamalesh Kholi. Elsevier Publication.
3. Statistical Methods for Clinical Trials, by Mark X Norleans, Marcel and Dekker, Inc, New York, 2001.

MPS2143: CLINICAL DATA MANAGEMENT (3 CREDITS)

1. **Introduction to Clinical Data Management** 2h

- History leading to GCDM
- Principles of DM
- Overview of key DM activities in clinical trials

2. **Regulatory considerations in DM** 3h

- 21 CFR Part 11 – Electronic Data Capture
- Good Clinical Data Management Practices (GCDMP)
- CDISC regulations

3. **CRF Design** Th– 4h, Pr -4h

- Protocol review
- Study design and impact on data collection
- Translating protocol summary to CRF data points
- *Practical sessions*
- Interpretation of protocol in CRF designing
- Paper based CRF designing
- eCRF designing
- Overview of CRF tracking

4. **Database setup and designing** 3h

- Clinical database concepts
- Database design and development
- Data entry applications design, development, validation and release
- Methods of data collection
- Paper CRFs
- Remote data collection
- Data validation during entry
- Specification Writing
- eCRF Specs
- Edit Specs – Front end and Backend
- Post production change request management

5. **Database validation** 2h

- Data validation programs
- Program specification
- Program development and validation
- Paper CRF Validation
- Edit check Validation
- Test Script Writing – Front End
- Test Script Writing – Back End
- Front End eCRF Validation
- Back end Validation

6. **Data Entry** 2h-Th, Pr - 2h

- Methods of data entry
- Single entry
- Double entry
- Fax imaged entry
- Data uploads
- Remote data entry
- Data entry errors and how to avoid them
- Single and Double Data entry in Paper Base trials
- Investigator training and monitoring for electronic CRF Data entry

7. **Data validation** 6h (Th – 3h; Pr – 3h)

- Validation principles - importance of clean data
- Data discrepancies - various types
- Edit checks - automatic checks
- Checks programs
- Manual data validation
- Query processing
- Drafting and finalization of standard and project specific guidelines
- Data Validation on continuous basis
- Visit and/or Subject wise Validation
- Validation per clinical specifications/milestones
- Practical sessions using dummy data

8. **Coding and dictionaries** 4h

- Coding concepts - why do we need coding
- Using dictionaries for coding
- Global dictionaries
- Automatic coding - the Autonecoder
- History and development of coding practices
- Different coding tools
- ESP Data Monitoring & Validation – i). External data handling of ECG, Radiology, LAB, etc.; ii). IVRS data handling
- SAE Reconciliation Pharmacovigilance related information training - SAE Reconciliation with the main database
- Practical session using MedDRA

9. Database lock and DM documentation 4h

- Understanding DB lock processors
- Timing of DB lock
- DM documentation - when and where
- Auditing DM documentation - preparation and process

1. Prelock data handling planning
2. Clean data check list etc…
3. Data base submission Filing of data per regulatory specifications and submission

10. Search, Collation & interpretation of published literature 6h
11. Research Data Presentation –Charts, Diagrams, Tables
12. Statistical Application

13. Scientific Writing for Publication
14. Clinical trial reporting – ICH E3

Books Recommended

1. Principal and practice of Pharmaceutical Medicine edited by Andrew j Fleteher. Lionel D Edwards, Anthony W Fox. Peter Stonier Published by John Wiley & sons Ltd.
2. Clinical Pharmacotherapeutics- edited by Kamalesh Kholi. Elsevier Publication.
3. Statistical Methods for Clinical Trials, by Mark X Norleans, Marcel and Dekker, Inc, New York, 2001.
4. Statistical issues in Drug Development by Stephen Senn, 1997, published by John Wiley and Sons Inc.
5. Practical and Clinical Applications 3rd Edn. Sandord Bolton, 1997 Marcel Dekkar Inc, Newyork.
6. Non parametric statistics for Behavioral Sciences by Sidney Siegel; 1956, McGraw Hills, New Delhi.
7. Design and Analysis of Bioavailability and Bioequivalence Studies – 2nd Edn. By Shein-Chung Chow and Jen-Pei Liu, 2000, Marcel Dekkar Inc, Newyork.
8. Computer Applications and Practicals: Introduction of softwares – SPSS/SAS and practical exercises.

Text Books

1. Pharmaceutical Statistics

MPS2101: BIOPHARMACEUTICS & PHARMACOKINETICS (3 CREDITS)

I. **Biopharmaceutical Considerations in Drug Product Design**

1. **Factors Influencing Dosage Form Design**:
   - i) Rate limiting step in Drug Absorption
   - ii) Biopharmaceutical Aspects
   - iii) Patient Considerations
   - iv) Manufacturing Considerations
2. **Factors Influencing Drug Dissolution/Bioavailability:**
   - i) Physico-Chemical
   - ii) Pharmaceutical, and
   - iii) Formulation
3. **Rate –Limiting Step in Bioavailability:**
   - i) Disintegration – in vitro, in -vivo
   - ii) *in-vitro* Dissolution Testing
   - iii) *in-vitro* Dissolution to *in-vivo* Absorption correlation including its failure.
   - iv) Dissolution Testing in lieu of Bioavailability Studies.

II. **Bioavailability & Bioequivalence**

1. Definitions of Related Terms (*UG)
2. Purpose of Bioavailability Studies (* UG)
3. Relative & Absolute Bioavailability
4. Bioavailability Assessment
5. Bioequivalence Studies
   - i) Design of Study ii) Statistical Evaluation
6. Waiver of *in-vivo* Bioavailability & Bioequivalence
   Biopharmaceutical Classification System (BCS) of Drugs
7. Ranking of Drugs and Several Formulations of the Drug

III **Biotransformation of Drugs**

1. Drug Metabolizing Organs and Enzymes
2. Chemical Pathways of Drug Biotransformation
   - i) Phase I reactions ii) Phase II reactions
3. Factors influencing Biotransformation
   - i) Physicochemical properties of the Drugs
   - ii) Chemical Factors
   - iii) Biological Factors

IV. **Drug Distribution & Elimination**

1. Physiological Factors Influencing Drug Distribution
2. Protein Binding
3. Volume of Distribution
4. Physiological Approach to Drug Elimination
5. Clearance Concepts
6. Dependence of Drug Elimination Kinetics on Clearance & Distribution

V. **Pharmacokinetics (based on Plasma & Urinary Excretion Data of Intact Drug)**

1. Compartmental Approach:
   - i) One Compartmental Model

ii) Two Compartmental Model

2. Non-compartmental Method

i) Single Oral Dose

ii) Multiple Oral Dose

Nonlinear (Dose Dependent) Pharmacokinetics:

i) Michaelis-Menten Concept

ii) Pharmacokinetics of Drugs under Such Situations

(One compartment model – single dose):

a) Intravenous Administration, and

b) First-Order Absorption

iii) Time-Dependent Pharmacokinetics

iv) Nonlinear Pharmacokinetics due to Protein Binding

v) Pitfalls in Pharmacokinetic Modelling

BOOKS RECOMMENDED

1. Wagner : Biopharmaceutics & Relevant Pharmacokinetics, Drug Intelligence Publication, 1971.
2. Swarbrick:Current Concepts in Pharmaceutical Sciences (Biopharmaceutics), Lea & Febiger, 1970.
3. Swarbrick: Current Concepts in Pharmaceutical Sciences (Dosage Form Design & Bioavailability), Lea & Febiger, 1973.
4. Niazi: Text Book of Biopharmaceutics & Clinical Pharmacokinetics, Appleton Century Crofts, 1979.
5. Evans et al.: Applied Pharmacokinetics (Principles of Therapeutic Drug Monitoring), Applied Therapeutics, 1980.
6. Gibaldi & Perrier: Pharmacokinetics, 2nd ed. (Revised & Expanded), Marcel Dekker (series in Drugs & Pharmaceutical Sciences – vol. 15), 1982.
7. Gibaldi: Biopharmaceutics & Clinical Pharmacokinetics, 3rd ed., Lea & Febiger, 1984.
8. Ritschel: Graphical Approach to Clinical Pharmacokinetics, 2nd ed., Prous Publishers, 1984.
9. Notari: Biopharmaceutics & Clinical Pharmacokinetics (an introduction), 4th ed. (Revised & Expanded), Marcel Dekker, 1987.
10. Rowland & Tozer : Clinical Pharmacokinetics (Concepts & Applications), 3rd ed., Lea & Febiger – Waverly, 1995.
11. Macheras et al: Biopharmaceutics of Orally Administered Drug, Ellis Horwood (series in Pharmaceutical Technology), 1995.
12. Welling & Tse: Pharmacokinetics (Regulatory, Industrial, Academic Perspectives), 2nd ed., Marcel Dekker (series in Drugs & Pharmaceutical Sciences-vol. 67), 1995.
13. Shargel & Yu: Applied Biopharmaceutics & Pharmacokinetics, 4th ed., Appleton & Lange, 1999.
14. Ratkowsky et al. : "Cross-Over Experiments: Design, Analysis & Applications," Marcel Dekker (series in Statistics: Textbooks and Monograph- Vol. 135)

MCR3101: PHARMACOVIGILANCE (3 CREDITS)

1. **Pharmacovigilance –**

i) Drug related problems in health care

Types and mechanisms of ADRs, Risk factors for ADRs, Drug – drug interactions, Other causes of drug related problems, Drugs in pregnancy and lactation, Management of patients affected by ADRs, Medication errors 5h

ii) Clinical manifestations of ADRs 5h

Drug related diseases affecting different organ systems (Brief Overview since covered in Clinical Pharmacology**)**

iii**)** Spontaneous reporting 5h

Organization, Setting up and running a PhV centre, Patient reporting, Managing individual case report forms, Terminologies, Feed back to reporters, Case assessment, Signal analysis and follow up, Root cause analysis of medication errors

iv) Epidemiological Methods 5h

Drug utilization studies, Cohort event monitoring, Cohort studies,
Case control studies, Longitudinal databases of patient records

v) Collection and management of safety data during clinical trials: 5h

Need for good quality safety information, Definition of good safety information, Differing regulations concerning safety data collection requirements, Designing a system to collect good quality information

vi) Post-marketing drug safety: Differences in clinical and post-marketing drug safety 4h

vii). Reporting to the Regulatory Authorities:
5h

Individual case safety reports, Periodic safety update reports, Answering queries from regulatory authorities, Updating product labelling – emphasis on safety changes, Safety reporting requirements, Safety report sources, Follow up of safety reports, Electronic safety reporting – Oracle & other software program available, Safety file retentions

viii) Global pharmacovigilance and safety standards 3h

- Background and introduction to pharmacovigilance
- The WHO and safety reporting
- CIOMS – function and purpose
- ICH – composition and guidelines
- MedRA

ix) Understanding signals and benefit-risk determinations 3h

- Definition of a signal
- Type of signal
- Who should be involved in signal detection process?
- Conducting signal detection in clinical and post-marketing surveillance
- Defining the signal in relation to risk/benefit
- Definitions of risk/benefit – FDA and EU perspective
- Risk/benefit assessments – who does this and where does the information go?
- Safety assessments and risk/benefit – frequency and reporting
- Changes in risk/benefit – how to manage and review existing profile

x) Standard operating procedures (SOPs) in relation to pharmacovigilance 3h

- Types of SOPs required
- Production and sign off of SOPs
- SOP maintenance
- SOP training

xi) The role of the qualified person (QP) 3h

- Contract versus permanent.
- Essential attributes of the QP
- The duties of the QP
- What the QP must do
- Internal audits of the company pharmacovigilance activities

xii) Audit

- Contracting out pharmacovigilance 3h
- Preparation for a regulatory inspection
- Scope of the pharmacovigilance inspection
- Conduct of the pharmacovigilance inspection
- The pharmacovigilance inspection report
- When things go wrong
- Corrective actions following a pharmacovigilance inspection

xiii) Narrative Writing – 3h

Books

1. Pharmacovigilance (2nd Edition) – Ronald D. Mann & Elizabeth B. Andrews, John Wiley & Sons
2. Pharmacovigilance from A to Z - Barton L. Cobert & Pierre Biron, Blackwell Science
3. Good Pharmacovigilance Practice – MHRA
4. Manual of Drug Safety and Pharmacovigilance – Barton L. Cobert, Jones & Bartlett Publishers
5. Dictionary of Pharmacovigilance – Amer Alghabban, Pahrmaceutical Press
6. An Introduction to Pharmacovigilance – Waller, Patrick; John Wiley & Sons
7. Pharmacovigilance (2nd Edition) – Ronald D. Mann & Elizabeth B. Andrews, John Wiley & Sons
8. Pharmacovigilance from A to Z - Barton L. Cobert & Pierre Biron, Blackwell Science
9. Good Pharmacovigilance Practice – MHRA
10. Manual of Drug Safety and Pharmacovigilance – Barton L. Cobert, Jones & Bartlett Publishers
11. Dictionary of Pharmacovigilance – Amer Alghabban, Pahrmaceutical Press
12. An Introduction to Pharmacovigilance – Waller, Patrick; John Wiley & Sons

MPSE111 DRUG REGULATORY AFFAIRS (3 CREDITS)

1. Concept and historical development of pharmaceutical product registration. Effect of GATT and WTO on commerce of pharmaceuticals Introduction to IPR, Schedule Y, NDA, ANDA. 6h
2. Globalization of drug industries, Export – in port policy of drug WHO certification. 6h
3. Batch Processing / Sample Analysis – Documentation & SOPs. 6h
4. 21 CFR Part 11 Compliance. 6h
5. FDA(21 CFR Part 320) / EMEA/ANVISA/Indian (CDSCO) Guidelines for BA / BE studies 6h
6. ICH QESM. 2h
7. GCLP Guidelines 4h

Books Recommended:

1. Guidance for preparing documents that meets Regulatory Requirements by Janet Gough.
2. FDA Regulatory Affairs by Donglas J Pisano & David Mantus.
3. FDA Guidelines.
4. ICH Guidelines.

MPS2142 QUALITY CONTROL LAB
(2 CREDITS)

1. Study of Components of GLP.
2. Study of documentation procedures in Quality Assurance.
3. Study of effect of change in solvent, pH on the U.V. Spectrum of given compound.
4. Comparison of I.R. Spectrum of compound and its derivative along with interpretation.
5. Study of drug-excipient interaction using DSC.
6. Study of Polymorphs using DSC
7. Analysis of Pharmacopoeial drug using HPLC.
8. Finger printing of Herbal preparation using HPTLC technique.
9. Evaluation of packaging material and containers.
10. Filling of Investigational New Drug (IND) as per FDA-format and registration detail.
11. Filling of Abbreviated New Drug Application (ANDA) as per FDA-format and registration.
12. Filling of Indian Patent Format & Procedure.
13. Study of Protocol preparation of Risk Management in Pharmaceutical Industries.
14. Study of Dissolution Profile for a given drug formulation.
15. Study of cases in the patent litigation of pharmaceuticals
16. Calibration and Validation of UV-Vis spectroscopy.
17. Calibration and Validation of IR spectroscopy.
18. Preparation of SOPs

MPS2144 BIOCHEMICAL ANALYSIS LAB
(2 CREDITS)

1. Determination of LD_{50} value.
2. Estimation of AST activity in serum.
3. Estimation of ALT activity in serum.
4. Estimation of ALP level in serum.
5. Estimation of Glucose level in serum.
6. Estimation of Cholesterol level in serum.
7. Estimation of Urea in serum.
8. Estimation of Urea in urine.
9. Estimation of Uric acid in serum.
10. Estimation of Uric acid in urine.
11. Estimation of Creatinine in serum.
12. Estimation of Creatinine in urine.
13. Estimation of SOD activity.
14. Estimation of Catalase activity.
15. Estimation of GSH levels.
16. Estimation of DPPH radical scavenging activity.
17. Isolation of DNA from Blood
18. Estimation of Lactate dehydrogenase in serum

Reference:

1. Biological standardization by J.H. Burn, D.J. Finney & L.G. Goodwin.
2. I.P. & B.P.
3. Screening Methods in Pharmacology – R.A. Turner.
4. Evaluation of drug activities by Laurance & Bacherce.
5. Methods in Pharmacology by Arnold Schwartz.
6. Selected topics on Experiment Pharmacology by Issha G. Kamat, Dadkar, N.K. & Seth, UK.
7. Fundamental of Experiment Pharmacology – M.N. Gl.
8. Pharmacological Experiment on intact preparation by Churchill Livingstone
9. Drug Discovery & Evaluation by Vogel HG.
10. Animal Model in Toxicology by Shayne Cox Gad & Christopher P, Chengelis.
11. Principles & Methods of Toxicology by Hays.
12. CRC Handbook of Toxicology by Derelako & Hollinger.

MPS 2146: CDM Lab. (Oracle Base) (2 CREDITS)

MPS 2148: SAS Lab. (2 CREDITS)

M. PHARM III SEMESTER (15 CREDITS)

MPS3141: Thesis:

- **Thesis Seminar**

M. PHARM IV SEMESTER (20 CREDITS)

MPS4141: Thesis:

- **Presentation, Submission and Viva-Voce**

BREADTH PAPERS

MMA1101: BIOSTATISTICS (3 Credits)

1. **Introduction:** 1h
   Relevance and the scope of Statistics.
   Difference between 'Descriptive' and 'Inferential' Statistics; Relationship between them

2. **Sampling Methods** 4h
   Introduction of sampling, probability and non probability sampling, sampling procedures – simple random, stratified, systematic, cluster and multistage sampling, concept of sampling distribution.

3. **Statistical Inference** 6h
   Statistical estimation – point and confidence interval estimations, Introduction of statistical hypothesis and testing, comparison of population mean with sample means, comparing two sample mans, comparison of population proportion with sample proportions, comparing two sample proportions, comparison of more than two samples, introduction of non parametric statistical tests.

4. **Correlation and linear regression** 6h
   Introduction of correlation & regression concepts, estimation of correlation coefficient, regression coefficients, assumption of tests of hypothesis in linear regression, variance of sample estimates of the parameters, confidence intervals in regression analysis, non linear regressions, weighted and transformations in regression analysis, application of linear regressions - standard curves in drug analysis and drug stability studies, analysis of covariance.

5. **Concepts of Inferential Statistics** 4h
   Basics of Statistical Inference
   Sampling distribution
   Estimation – Point estimation, Interval estimation
   Parameter, Statistic, Concept of a hypothesis, Research Hypothesis, Null Hypothesis, Level of Significance, Comparison of means of two samples, Comparison of sample proportion with population proportion, Comparison of two sample proportions,
   Degrees of Freedom, Critical Value, Table value, Type I and Type II errors, Rules for rejection & acceptance of Null Hypothesis, Standard Error

6. **Inferential Statistics - Parametric Test**: 4h
   't' test – Comparison of sample mean with the population mean, Comparison of means of two independent samples, Comparison of two correlated samples
   'Z' test – different applications
   Annova – one way annova: 'F' test

7. **Quality control:**
   Introduction, control charts, acceptance sampling and operating characteristic curves, statistical procedures in Assay.Department, establishing in-house limits, some statistical aspects of quality and the "Barr Decision".

8. **Inferential Statistics - Non-parametric test**: 2h

Chi square test- Testing of goodness of fit, testing of independence, Test of homogeneity; Wilcoxon signed rank test; McNemar test

9. **Computer Applications & Practicals:** 2h
   Introduction of statistical software – SPSS with practical exercises

BOOKS RECOMMENDED:

1. Statistical issues in Drug Development by Stephen Senn, 1997, published by John Wiley and Sons Inc.
2. Practical and Clinical Applications 3rd Edn. Sandord Bolton, 1997 Marcel Dekkar Inc, Newyork.
3. Non parametric statistics for Behavioral Sciences by Sidney Siegel; 1956, McGraw Hills, New Delhi.
4. Design and Analysis of Bioavailability and Bioequivalence Studies – 2nd Edn. By Shein-Chung Chow and Jen-Pei Liu, 2000, Marcel Dekkar Inc, Newyork.
5. Computer Applications and Practicals: Introduction of softwares – SPSS/SAS and practical exercises.

Text Books

1. Pharmaceutical Statistics

MPS1003: BIOLOGICAL STANDARDIZATION & PHARMACOLOGICAL SCREENING (3 Credits)

1. Laboratory Animals 7h.
   a. Commonly used laboratory, transgenic and other genetically prone animal models (viz. nude mice SH rats etc.)
   b. Techniques of blood collection, anesthesia & euthanasia of experiment animals.
   c. Maintenance & breeding of laboratory animals.
   d. Regulation and ethics requirements.
   e. Guidelines & regulatory agencies – CPCSEA, OECD, FDA ICH, FHSA, EPA, EEC, WHO, etc.
   f. Importance of alternative experimental models, its advantages & disadvantages.

2. Principles of Biological Standardization 4h.
   a. Methods of biological assay, principles of biological assays with certain examples as per IP and BP.
   b. Development of new bioassay methods.

3. Immunoassay 5h
   a. General principles of immunoassay, Theoretical basis, Optimization of immunoassay, Heterogenous immunoassay system, Homogenous immuno system.
   b. Production of immunoassay reagent: Introduction, receptors or binders, unlabelled ligands Calibrators, Labelled ligands and receptor, Separation technique, buffers.
   c. Immunoassay Methods Evaluation: Protocol outline, objective & preparation, evaluation of precision, standard tracer, sensitivity, evaluation of accuracy, antibody characteristics, monitoring, reaction conditions, clinical evaluation.

4. Organization of screening for the Pharmacological activity of new substances with emphasis on evaluation using in-vivo, in-vitro, ex-vivo, in-situ, in silico and other possible animal alternative models. 18h.

   a. General Principles & safety pharmacology procedure.
   b. CVS Pharmacology – Antihypertensive, Anti arrhythmics, Vasodilators, disentail.
   c. CNS Pharmacology – behavioral & muscle co-ordination, CNS stimulants, anti-epileptics, Nootropics.
   d. Drugs for Neurodegenerative diseases, like parkinsonism, Alzheimers, multiple sclerosis.
   e. Drugs acting on ANS.
   f. Respiratory Pharmacology – Anti-asthmatics, COPD, Anti-allergic & Mucoactives.
   g. Reproductive Pharmacology – Aphrodisiacs & antifertility agents.
   h. Analgesics, anti-inflammatory & antipyretics.
   i. G.I.T. – Anti-ulcer, anti-emetics, anti-diarrhoeal & laxatives.
   j. Anti-cancer agents.
   k. Metabolic disorders like anti-diabetics, anti-hyperlipidemic, anti-obesity, hepatoprotective.
   l. Models in drug absorption & metabolism.
   m. Immuno Pharmacology – specific (cell & hormonal mediated) & non-specific methods.
   n. Screening of free radical scavenging activity.
   o. Acute, Sub-acute & Chronic toxicity test.

5. Clinical pharmacology and pharmacodynamics: clinical study design, documentation, presentation and interpretation 2h

6. Clinical trials: definition, phase I – IV studies, design documentation, presentation and interpretation, statistical analysis of clinical data, factorial design, guidelines as per Indian and other regulatory authorities. 7h

BOOKS RECOMMENDED :

1. Biological standardization by J.H. Burn, D.J. Finney & L.G. Goodwin.
2. I.P. & B.P.
3. Screening Methods in Pharmacology by R.A. Turner. Vol. I & II Academic Press, New York and London.
4. Evaluation of drug activities by Laurence & Bacherce.
5. Methods in Pharmacology by Arnold Schwartz.
6. Selected topics on Experiment Pharmacology by Issha G. Kamat, Dadkar, N.K. & Seth, UK.
7. Fundamental of Experimental Pharmacology, by M..N. Ghosh. Scientific Book Agency, Calcutta.
8. Pharmacological Experiment on intact preparation by Churchill Livingstone
9. Drug Discovery and evaluation by H.G. Vogel & W.H. Vogel. Springer Verlag, Berlin Heideleberg.
10. Animal Model in Toxicology by Shayne Cox Gad & Christopher P, Chengelis.
11. Principles & Methods of Toxicology by Hays.
12. CRC Handbook of Toxicology by Derelako & Hollinger.
13. Handbook of Experimental Pharmacology by S.S. Kulkarni. Vallabh Prakashen, Delhi.
14. Pharmacological Experiments on Intact and Isolated preparations, Edinburgh University Pharmacology Staff, Livingstone.
15. Goodman and Gilman's The Pharmacological basis of Therapeutics – Ninth edition, Editors. A. G. Gilman, J. G. Hardman, L. E. Limbiod, P. B. Melineff, R. W. Rudder, Macmillan Publishing Co. Inc. – Latest edition.
16. Clinical Pharmacotherapecutics, edited by Kamalesh Kohli, Elsevier Publication.