M.Sc. in Clinical Research

CLINICAL RESEARCH PROGRAMS

DEPT. OF MICROBIOLOGY

SCHOOL OF SCIENCES

GUJARAT UNIVERSITY

M.Sc. in Clinical Research

Course Outline

Semester I			
Module I	MSCCR101	Elements of Microbiology & Biotechnology	70 hrs
Module II	MSCCR102	Fundamentals of Anatomy, Physiology & Pathophysiology	70 hrs
Module III	MSCCR103	General Pharmacology & Pharmacokinetic & Pharmacodynamic of Drugs	70 hrs
Semester II			
Module IV	MSCCR201	Pharma-Medicine & Clinical Research	70 hrs
Module V	MSCCR202	Regulations in Clinical Research	70 hrs
Module VI	MSCCR203	Clinical Research Operations Management	70 hrs
Semester III			
Module VII	MSCCR301	Conduct of Bioequivalence Studies	70 hrs
Module VIII	MSCCR302	Clinical Data Management & Biostatistics	70 hrs
Module IX	MSCCR303	Pharmacovigilance & Post Marketing Surveillance	70 hrs
Semester IV- MSCCR401 Dissertation			

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SEMESTER I

MODULE I: ELEMENTS OF MICROBIOLOGY & BIOTECHNOLOGY 70 hrs

Basic Microbiology

- Science of Microbiology
- Structure of prokaryotic cell, virus
- Methods in Microbiology-viewing, measuring, culturing and preservation of microorganisms
- Growth of microbes
  - ✓ Growth type / rate / phases
  - ✓ Nutrients for microbes and their transfer
- Control of microorganisms
  - ✓ Death rate, sterilization
  - ✓ Physical controls
  - ✓ Chemical controls

Basic Biotechnology

- Introduction to bacterial genetics and rDNA technology
  - o DNA, RNA, protein composition and structure
  - o Transcription and translation
  - o Gene regulation
  - o Introduction, and molecular biology tools for rDNA technology
  - o Methods of gene transfer and plasmid technology
  - o Guidelines for genetic engineering
- Basic techniques in rDNA technology PAGE, DNA isolation and purification, blotting techniques, PCR, nucleic acid sequencing
- Introduction to animal biotechnology - transgenic animals
- Biotechnology derived drugs and their processes

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Clinical microbiology

- Host parasite interaction
    - ✓ Microorganisms and human diseases - properties and capacities of selected pathogens
        - ✓ Basic aspect of immune systems
        - ✓ Diagnostic immunology
        - ✓ Prevention of microbial diseases – an overview

Quality control and assurance

- Biotechnology - society, risks, ethics, patenting
- Biosafety guidelines
- Role of culture collection centres, public health laboratories and regulatory agencies
- National accreditation board for laboratories
- Bioethics principles, international codes and guidelines in India
- Role of regulatory bodies involved in testing and approval of biotechnology derived drugs

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MODULE II: FUNDAMENTALS OF ANATOMY, PHYSIOLOGY & PATHOPHYSIOLOGY 70 hrs

- **Basics of Anatomy & Physiology:** Cells, tissues, structure and functions
- **Blood**: Plasma, erythrocytes, hemoglobin and anemia, leucocytes, thrombocytes, coagulation of blood, blood groups and transfusion, immunity, tissue macrophage system and lymph
- **Nerve**: Nerve biophysics, Neuron, Nerve conduction and classification of nerve fibers
- **Muscle**: Skeletal muscle structure and mechanism of contraction, Mechanism of muscle contraction, Neuromuscular transmission
- **Cardiovascular System**: Anatomy of the heart, Circulatory system including Arterial and Venous system with special reference to the names and positions of main arteries and veins, Properties of Cardiac muscle, Blood pressure and its regulation, Renin Angiotensin system and its significance, Physiology of cardiac muscle, cardiac impulse, electrocardiogram, cardiac cycle, heart sounds, heart rate and its regulation, cardiac output, arterial pulse and venous pulse, cardiovascular changes in muscular exercise, circulatory shock, cardiac failure
- **Respiratory System**: Anatomy of Respiratory organs, Functional anatomy of respiratory system, mechanics of respiration, lung volumes and capacities, dead space, alveolar ventilation and diffusion of gases, parameters like VC, TC, FEV, transport of oxygen, transport of carbon dioxide, regulation of respiration, artificial respiration
- **Excretory System and Body Fluids**: Various parts of urinary system and their functions, Structure and functions of Nephron, formation of urine, micturition, renal function tests, electrolyte balance, juxtaglomerualr apparatus, body fluids, skin and body temperature, metabolic function of liver, gall bladder and related glands, mechanisms of excretion
- **Endocrine Glands and Reproduction**: Role of Endocrine Glands in Regulation and Integration of various functions of the Body, Anatomy and Physiology, General considerations, pituitary gland, thyroid gland, endocrine regulation of calcium and phosphorus metabolism, parathyroid gland, islets of langerhans, adrenal gland,

prostaglandins, thymus and pineal gland, female reproductive system, male reproductive system

- **Nervous System**: Divisions of Nervous System, Central Nervous System (Brain & Spinal Cord), Reflex action, Electroencephalogram (EEG), Overview of Neurotransmitters, Peripheral Nervous System (PNS) (Cranial nerves & spinal nerves)Synaptic transmission, sensory receptors, pain, reflex action, spinal cord, thalamus, cerebellum, cerebral cortex, Sleep, hypothalamus, cerebrospinal fluid, autonomic nervous system
- **Digestive System**: Organization of digestive tract, digestive secretions, gastrointestinal hormones, liver, gastrointestinal motility, absorption of food
- **Special Senses:** Vision, hearing, chemical senses
- **Fundamentals of Pathophysiology:** Derangement of Homeostasis and hemodynamics, Definition, terminology, pathology of following diseases including etiology, risk factors, signs and symptoms, overview of treatment and diagnosis of the disease
- **Diseases**- Systemic pathology of blood vessels and lymphatics, liver, exocrine pancreas, kidney, endocrine system, musculoskeletal system, nervous system, system associated diseases like Hypertension, congestive heart failure, cardiac arrhythmias, ischemic heart diseases, obesity, atherosclerosis, bronchial asthma, chronic pulmonary obstructive disease, tuberculosis, peptic ulcer disease, inflammatory bowel disease, HIV infection and AIDS, hepatitis, anemia, Type 1 and type 2 diabetes, cancer and its types, rheumatoid arthritis, schizophrenia, depression, migraine, anxiety, insomnia, normal ranges of laboratory parameters

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MODULE III: GENERAL PHARMACOLOGY & PHARMACOKINETIC & PHARMACODYNAMIC OF DRUGS 70 hrs

- **General Pharmacology-:** Introduction, scope and branches of pharmacology, sources of drugs and nomenclature of drugs, dosage forms, Routes of drugs administration and drug delivery systems, factors modifying drug action, tolerance and dependence, dynamics of absorption, distribution and excretion of drugs, Basic pharmacokinetic parameters employed in the use of drugs, their bioavailability and biotransformations, metabolizing enzymes as targets of drugs action- enzyme induction and inhibition, biological half life and its significance, Models of pharmacokinetics, Pharmacodynamics-mechanism of drug action, site of drug action, drug receptor interaction types of receptors, Bioavailability and Bioequivalence, Drug antagonism and synergism, dose response relationship, drug dependence, Adverse drug effects and their monitoring, Iatrogenic diseases, Pharmacogenomics, pharmacoeconomics
- **Overview of Drug Pharmacology:** Current interventions, classification of drugs, pharmacokinetics, therapeutic effects, mechanism of action, adverse effects and contraindications, dose, marketed preparations of the following class of drugs
- **Drugs acting Central Nervous System(CNS):** Autonomic and somatic transmission, General anesthetics, anxiolytics and hypnotics drugs, anti depressants, CNS stimulants and psychotomimetic drugs, Opioid analgesics and opioid anatagonists, Drug dependence and drug abuse, Antiepileptic drugs, Drug therapy for neurodegenerative disorders like parkinson's disease and schizophrenia
- **Drugs acting on Autonomic Nervous System (ANS)**: General introduction, Parasympathomimetic, parasympatholytic, Sympathomimetic, sympatholytic agents, Ganglionic stimulants, blockers and adrenergic neuron blocking drugs, local anesthetics
- **Drugs acting on Cardiovascular System (CVS)**: Cardiac glycosides and positive ionotropic agents, Anti-arrhythmic drugs, Antihypertensive drugs, Coronary vasodilators and drugs used in angina, Anti-hyperlipidemic drugs, Fibrinolytic agents, Cardioprotective agents, Anti-anginal agents

- **Antihypertensives**: Overview, classification of antihypertensive drugs- Diuretics, Sympatholytics, angiotensin inhibitors, vasodilator, dopamine agonists
- **Drugs acting on Respiratory System**: Expectorants, Anti-tussive bronchodilators, Drugs used in common cold
- **Anti Cancer:** Types of cancer, etiology of Cancer , drugs used in cancer chemotherapy, toxicities of drugs used in cancer chemotherapy, resistance to cytotoxic drugs, Preferred combination chemotherapy for certain malignancies
- **Anti Diabetic:** Insulin preparation, types of diabetes, Antidiabetic drugs: Sulfonylurea drugs, Meglitinide drugs, Alpha-glucosidase inhibitors, Biguanide, thiazolodinediones
- **Non Steroidal Anti-Inflammatory Drugs(NSAIDS):** Classification of NSAIDS, Mechanism of action , NSAIDSwhich do not inhibit prostaglandin synthesis
- **Anti-Coagulants, Antiplatelet and Fibrinolytic Drug:** Normal hemostatis, anticoagulant drugs, parenteral anticoagulants, antiplatelet drugs, fibrinolytic drugs
- **Chemotherapy of Microbial Diseases:** Introduction to chemotherapy, Sulfonamides, Qinolones and treatments of urinary tract infection, Penicilins, cephalosporins and other β- lactum antibiotics, Aminoglycosides, Microlides, other antibacterial drugs, broad spectrum antibiotics: Tetracyclines and chloramphenicol, Chemotherapy of tuberculosis and leprosy

REFERENCES FOR READING

- Elements of Human Anatomy Physiology & Health Education by Dr Ramesh Goyal
- Elements of Pharmacology by Dr Ramesh Goyal, Dr. Anita Mehta
- Handbook of Pathophysiology by Joan P Frizzell
- Text Book of Pathophysiology by Dr. Rajpal Bansal, Dr. Anu Gupta
- Anatomy and Physiology in Health and Illness by Anne Waugh, Allison Grant
- Human Anatomy Vol 1, Upper Limb & Thorax by B D Charuasia's
- Human Anatomy Vol 2 Lower Limb, Abdomen & Pelvis by B D Charuasia's

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- Human Anatomy Vol 3, Head, Neck & Brain by B D Charuasia's
- Textbook of Physiology for Dental Students by H V Tandan , R Chandramouli
- Color Atlas of Pharmacology Ebooks by Heinz Lullmann, Kaus Mohr, Luts Hein, Detlef Bieger
- Basic and Clinical Pharmacology by Katzung B
- Pharmacology by Brenner G
- Principles of Pharmacology by Golan D
- Principles of Pharmacology by Sharma H
- Pharmacology for the Health Care Professions Ebook by Christine M Thorp

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SEMESTER II

MODULE IV: PHARMA-MEDICINE & CLINICAL RESEARCH 70 hrs

- **Drug Discovery**: Drug design-Ligand ba**se**d, Structure based, Active site identification, rational drug discovery High throughput screening, Structure Activity Relationship (SAR), Quantitative Structure Activity Relationship (QSAR), Computer assisted drug designing (CADD)
- **Phases in Clinical Development of Drug** : Terminology in clinical research, Preclinical phases, First in human trials, Single ascending dose and multiple ascending dose studies, Exploratory clinical trials, Confirmatory clinical trials, post marketing surveillance
- **Preclinical Study Guidelines** : Non clinical overview and non clinical summaries(M4S(R2)), Non clinical safety studies(M3(R1)), Guidance on non clinical safety studies for the conduct of Human clinical trials and marketing authorization, Dose response information to support drug registration(E4), Clinical safety data management, guideline on the need of carcinogenicity studies of pharmaceuticals(S1A), Duration of chronic toxicity testing in animals (rodent and non rodent toxicity testing (S4), safety pharmacology studies for human pharmaceuticals (S7A), Non clinical evaluation for anti cancer pharmaceuticals (S9)
- **History & Background of Origin of Clinical Research:** Thalidomide tragedy, Sulphanilamide disaster, WMA Declaration of Helsinki- Ethical Principles for Medical Research Involving Human Subjects, The Belmont Report
- **Types of trials:** Pharmacoepidemiology, Meta-analysis, Case control study, Prevention Trials, diagnostic trial, Treatment trial, Case cohort study, Observational studies, Quality of life trials
- **Fundamentals of Trial Design –** Randomized clinical trial, uncontrolled trials, protocol development, end points, Patient selection, sources and control of bias, Randomization, sample size and power
- **Clinical/Contract Research Organizations(CRO)** - Definition, fundamental operations of CRO, Role and responsibilities of CRO, Organogram of CRO, basic documentation in

CRO, Site Management Organizations (SMO), Central Lab, Research Management Organizations and differences between Contract Research Organization/Site Management Organization/Research Management Organization, Functions of Quality Assurance and Quality Control Departments, Bioanalytical Departments, Clinical Project Management, Regulatory affairs, Medical Writing and Data Management, Biostatistics

- **Study Execution Process-** Study design, Feasibility, Overview of National regulatory applications, CR professional training and development, preparations and planning for clinical trials, CRF and monitoring, Training and site management**,** Budget Management of Clinical trials

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MODULE V: REGULATIONS IN CLINICAL RESEARCH 70 hrs

- **Ethical Aspects:** Ethical principals underlined research involving human subjects, respect for persons, beneficence, justice, legal authorities for Institutional Review Board (IRB), Heath and Human Services regulations(HHS) , FDA regulations, regulatory requirements, duties of IRBs, IRB membership, role of IRB in reviewing Clinical Drug Trials, Assessment of scientific design, competence of investigator, selection of subjects, balancing benefits and risks , Compensation for research related injuries, special issues like role of Lay member of IRB, review of multi institutional trials, duty to monitor, financial risks of clinical trial subject, compliance with new regulations
- **History of Good Clinical Practices (GCP):** Introduction to ICH-International Conference on Harmonization of technical requirements for registration of Pharmaceuticals for human use guidelines Milestones in the evaluation of GCP , The Nuremberg Code, Principles of ICH-GCP
- **Applicable GCP Guidelines:** International Conference on Harmonization of technical requirements for registration of Pharmaceuticals for human use guidelines (ICH-GCP), Indian Council Of Medical Research- Ethical Guidelines for Biomedical Research on Human participants (ICMR), Indian Good Clinical Practices
- **International Regulatory bodies and Guidelines**:
  - ***US Food and Drug Administration(USFDA):*** The FDA and Food Drug and Cosmetics Act, New drug development and approval : the principal steps
  - ***India****:* Regulatory laws, Schedule Y, registration of new drugs, requirements for registration, regulatory environment and practices
  - ***Medicines and Healthcare Products Regulatory Agency (MHRA)***: Overview of regulatory environment/ background, regulatory authorities, regulatory requirements and procedures
  - ***European Agency for Evaluation of medicinal Products(EMEA)***: National registration , the decentralized procedures, mutual recognition procedures
  - ***Brazil*****:** Overview of regulatory affairs

- ***Good Laboratory practices(GLP) :*** Organization and Personnel, Quality assurance program, Facilities, Equipments, reagents and Materials, Standard operating procedures, Storage of Records and Reports

- **Council for International Organizations of Medical Science (CIOMS) guidelines:** CIOMS International Ethical guidelines for biomedical research involving human subjects, Principles Of Medical Ethics Relevant To The Protection Of Prisoners Against Torture (1983)
- **Intellectual Property Rights:** Terminology, Patent Laws, TRIPS (Trade Related Intellectual Property Rights) Agreement, Trademarks, copyrights
- **Clinical Trial Application Requirements**
  - **Investigational New drug (IND):** Classifications, IND application submission check list, FDA IND review check list , IND application process, Information for sponsors-investigator submitting IND, IND forms and instructions
  - **New Drug Application(NDA)**: Pre NDA meeting , NDA submission Check list , FDA NDA review check list
  - **Abbreviated New drug Application(ANDA):** ANDA content, ANDA Submission check list , FDA ANDA review check list , ANDA process for generic drugs, guidance documents for ANDAs, ANDA forms and electronic submissions
  - **Orphan Drugs Application :** Submission check list, FDA orphan drug review check list , FDA documents

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MODULE VI: CLINICAL RESEARCH OPERATIONS MANAGEMENT 70 hrs

- **Operation in CRO & SMO**
    - **Site Selection Criteria**- Site Selection parameters: Location, Staffing, Qualifications, History, Clinical trial experience, Area of therapeutic experience, Investigational pharmacy, ICH-GCP compliance, Patient enrollment, Site Selection Check list, Site Initiation Visit (SIV)
    - **Single Centre/Multi Centre Trial**- Definition, benefits of Single centre and or Multi centre, Differences between Single centre & Multi centre Trial
    - **Investigator Selection**

      Investigator qualification and agreement, duties delegation, Undertaking by the Investigator, Feasibility study, Other functions-Central lab, Shipment and shipping records, meetings with Sponsor, analysis & interpretation of results etc
- **Operation of Institutional Review Board (IRB)/ Independent Ethics Committee (IEC) -** Defining Scope of IRB/IEC Authority**,** Responsibilities of IRB/IEC, Composition of IRB/IEC, Basic Functions, Operation and Procedure of IRB/IEC, Communication with IRB, IRB/IEC Records, Documents for submission to IRB/IEC, Difference between IRB and IEC
- **Roles & Responsibilities of Clinical Trial Personnel**
    - Roles & Responsibilities of Sponsor
    - Roles & Responsibilities of Investigator
    - Roles & Responsibilities of CROs/SMOs
    - Roles & Responsibilities of CRA/Monitor
    - Roles & Responsibilities of Auditor
    - Roles & Responsibilities of Clinical Research Coordinator
    - Roles & Responsibilities of Clinical Data Manager
    - Roles & Responsibilities of Clinical Biostatistician

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- **Clinical Trial Documentation:**

- **Investigator's Brochure**- Confidentiality Statement, Summary, Introduction, Physical, Chemical, and Pharmaceutical Properties and Formulation, Nonclinical Studies, Nonclinical Pharmacology, Pharmacokinetics and Product Metabolism in Animals, Toxicology, Effects in Humans, Pharmacokinetics and Product Metabolism in Humans, Safety and Efficacy, Marketing Experience, Summary of Data and Guidance for the Investigator
- **Study Protocol -** The contents of a trial protocol should generally include the topics: General Information, Background Information, Trial Objectives and Purpose. Trial Design, Selection and Withdrawal of Subjects, Treatment of Subjects, Assessment of Efficacy, Assessment of Safety, Biostatistics, Direct Access to Source Data/Documents, Quality Control and Quality Assurance, Ethics, Data Handling and Record Keeping, Financing and Insurance, Publication Policy, Supplements, Annexure
- **Case Report Forms (CRF) & e-CRF-** Study Title, Inclusion Criteria, Exclusion Criteria, Patient Screening, Admission /discharge procedure, Visit wise, Period wise, Laboratory Analysis, Vital signs, Diet restriction, Concomitant medication, withdrawal/drop out details, Adverse Events Form, Serious Adverse Event Form
- **Informed Consent Form/Assent Form-** Study title, What is the purpose of research, The study design, Study Procedures, Women of childbearing potential, Possible risks , Possible benefits, Compensation, Possible benefits to other people, The alternatives you have, Cost to the participant, Confidentiality of the information of subject/patient, decision to participate/ not participate, Withdrawal of the consent, Right to new information, Contact persons, Patient consent form, Patient Information Sheet, Patient visit diary
- **Clinical Study Report-** Title Page, Synopsis, List Of Abbreviations And Definitions Of Terms, Ethics, Investigators And Study Administrative Structure, Introduction, Study Objectives, Investigational Plan, Study Patients, Efficacy Evaluation, Efficacy Evaluation, Discussion And Overall Conclusions, Tables, Figures and Graphs Referred, Reference List, Appendices

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- **Standard Operating Procedures (SOP) in Clinical Trials** - Need of SOPs, What is SOPs, Benefits of SOPs, different types of SOPs, SOP Writing SOPs and Guideline, Implementation and monitoring of SOPs, Change control
- **Essential Documents-**Importance of Essential Documents
    - **Pre Study Document**: Investigators Brochure, Financial aspects of the trial, Approval letter from the IRB, IRB Composition etc
    - **During the Study Documents**: Updates on medical/laboratory/technical procedure tests, Investigational product(s) accountability at site, Subject enrolling log, Audit certificate etc
    - **Post Study Documents**: Final report by investigator to IRB, Final report by investigator to regulatory authorities, Clinical study report to document results and interpretation etc, Study Completion documents, Study Termination/closure documents
- **Procedures in Clinical Trial**
    - **Quality Assurance and Quality Control in Clinical Research** –Introduction, Regulatory requirement of quality Assurance(QA) and Quality Control (QC) in Clinical Research, Role and Responsibilities of QA personnel, Different types of Audit, Quality System and Quality Policy, Continual Process Improvement
    - **Interventions, Study Drug Packaging and Distribution** Study Drug Receipt, Dispensing, Accountability, Storage, Disposal, Regulatory Requirement. An over view of clinical trial interventions, describe issues related to study drug packaging and masking, discuss logistics of study drug distribution, and describe treatment adherence in clinical trial
    - **Monitoring in Clinical Trials**: Purpose of monitoring & Monitor's responsibilities, Selection and qualification of monitors, Monitoring procedures, Monitoring report, Audit, Extent and nature of monitoring , Medical Monitoring, Query Resolution

- **Project Management and Business Development:** Skills of Business Development personnel, Roles and responsibilities of a Project manager, Project Management matrix, Business development strategies

REFERENCES FOR READING

- Business Development for the Biotechnology and Pharmaceutical Industry by Martin Austin
- Clinical Drug Trials & Tribulations Ebooks by James Swarbrick
- Clinical Research Coordinator Handbook Ebook by Deborah Rosenbaum, Michelle Dresser
- Clinical Trial Medicine Ebook by Richard Chin, Bruce Y. Lee
- Clinical Studies Management by Simon Cook
- Clinical Trials – Ebooks by Duolao Wand, Ameet Bakhai Remedica
- Good Clinical Practice by Josef Kolman, Paul Meng
- Guideline for Drug Regulatory Submissions by Sandy Welnberg
- International Pharmaceutical Registration by Alan A Chalmers
- International Research in Health Care by Felicity Smith, Sally Anne Francis, Ellen Schathecutle
- Quality Management in Clinical Trial Research Ebook by Graham D. Ogg
- Pharmaceutical Biotechnology by O Kayser, R H Muller

PRACTICAL EXERCISES & EXPOSURE

- Case studies solutions
- Technical and soft skill presentations
- Term search
- Development of Clinical research documents
  - SOPs development
  - CRFs & ICFs Preparation

- Dummy clinical research and bioequivalence protocols etc,

- Role plays of real clinical research stake holders like Clinical research associate, investigator, project manager, volunteer, clinical research coordinator, auditor etc

INDUSTRIAL EXPOSURE

During initial visit an overview of the facility infrastructure, flow of activity, visiting different areas like screening room, medical examination room, phlebotomy room, dining area, baggage and body area, clinical pharmacological unit, dosing area, investigator`s cabin, drug store, plasma separation and storage room.

On site exposure which includes observation of actual in-process activities like blood collection, plasma separation, screening of volunteers, informed consent process.

A visit to Analytical Department and Central Laboratory to have know-how of the tests/investigations conducted and other procedures performed in respective departments

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SEMESTER III

MODULE VII: CONDUCT OF BIOEQUIVALENCE STUDIES 70 hrs

- **Introduction to Bioavailability & Bioequivalence**- Basic Definitions, Requirements of Bioavailability and Bioequivalence study, Study Design, Bio statistical procedure, Bio analytical method and Method validation, submission of study to the regulatory, Bioequivalence and Pharmacokinetics
- **Guidelines of Bioavailability (BA)/ Bioequivalence(BE) Studies**
  - **USFDA guideline**- Introduction, Background, Methods to document BA and BE, Comparison of BA measures in BE studies, Documentation of BA and BE, Special topics, General pharmacokinetic study design and data handling
  - **ANVISA guideline**- Introduction, Background, Acceptance Criteria of BA/BE Unit, General Consideration for BA/BE study, Guidance for Protocol Design of BA/BE study, Guidance for report preparation of BA/BE study
  - **Overview of International BABE guidelines:** Therapeutic Goods Administration **(**TGA) guideline, Therapeutic Product Directorate **(**TPD) guideline, European Agency for Evaluation of medicinal Products (EMEA) guideline
- **Regulatory Submissions**: Drugs Controller General of India (DCGI)/Central Drugs Standard Control Organization (CDSCO) submissions, Directorate General of Foreign Trade (DGFT), T-License, e-CTD (Common Technical Document)
- **Difference in various Bioavailability (BA)/ Bioequivalence (BE) Guidelines**- Different Regulatory Bodies and differences in terms of: Selection of Reference Product, Drug content / potency, Number of subjects, Inclusion Criteria, Exclusion Criteria, Dosing Water Quantity. Water restriction and food restriction, requirement of Fed Study, Minimum sample points, Length of blood sampling time, Washout, Metabolites concentration measurement, Drugs with non-linear Pharmacokinetic, Drugs with Long Half-life, Modifies release formulation, Withdrawal /dropout criteria, Outliers, Retention period for Study Drugs sample

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- **Conduct of Bioequivalence study**- Role of Different Departments involve in Bioequivalence study (Business development, Screening department, Clinical department, Bio-analytical department etc), Life span of Bioavailability and Bioequivalence study(BABE study), day to day activity during the study
- **Operations in BABE**: Role of Quality Assurance & Quality Control in BA/BE studies, Role of Medical Writing in BA/BE studies, Waiver of BA/BE Studies, Role of Project Management and Business development in BA/BE studies

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MODULE VIII: CLINICAL DATA MANAGEMENT & BIOSTATISTICS 70 hrs

- **Introduction to Clinical Data Management(CDM):** Definition, Steps in CDM, Data management process and work flow, Code of Ethics for CDM professionals **,** CDM and case record form (CRF), needs of CRF users, standardization of CRFs, guidelines for designing CRF
  - **Data Entry/Remote data entry**: First data entry, Second data entry, heads up and heads down data entry, audit trail, 21CFR part 11, computerized system in clinical trials, QAQC in data entry
  - **Data Tracking**: Tracking CRF pages and corrections, CRF work flow, tracking challenges, tracking of query forms
  - **Data Capture:** Definition, paper based and electronic data capture, dataflow in paper CRFs and e-CRFs, tools for data capture, advantages and disadvantages of paper CRF/ e-CRF
  - **Data Coding**: Definition, data quality, coding significance, coding dictionaries, Coding symbols for a thesaurus of adverse reaction terms (COSTART), problems with Coding data, special search categories, coding of AE data
  - **Data cleaning/validation**: Definition, Discrepancy management system, edit check specifications, query management, cleaning data checklist, SAE reconciliation, managing laboratory data, data locking/freezing
  - Overview of Data management Software(s)
- **Introduction to Biostatistics & its role in Clinical Research:** Population & Sample, Parameter & Statistic, Types of variables, Measures of Central Tendency-Mean, different types of mean, Median, Mode, Histograms, Scatter Plots, Construction & Labeling of graphs, Normal & Binomial Distribution, Research Hypothesis testing, Sample size calculation & Power, p-value, Confidence Interval, Randomization methods, Blinding in Clinical research

- **Parametric tests & Non-parametric tests and its applications:** t-test, Z-test, chi-square test, ANOVA, ANCOVA, Spearman's correlation coefficient test, Wilcoxon Rank Sum Test, Kruskal-Wallis test, Rank correlation, linear regression & correlation

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MODULE IX: PHARMACOVIGILANCE & POST MARKETING SURVEILLANCE

70 hrs

- **General overview of Pharmacovigilance:** Introduction, Definitions**,** Adverse Event (AE), Adverse Drug Reaction(ADR), Serious Adverse Drug Reaction (SAE), Unexpected Adverse Reaction, Suspected-unexpected serious Adverse reaction (SUSAR), Signal and Detection of Signal, Diagnosis and management of adverse drug reactions, Periodic safety Update Report(PSUR), Individual case safety report, Spontaneous reporting, Risk Evaluation and Mitigation Strategy, Significance of Pharmacovigilance, Audit in Pharmacovigilance
- **Pharmacovigilance and ICH guideline:** ICH-E2A Clinical Safety Data Management – Definitions and Standards for Expedited Reporting, ICH-E2C Clinical Safety Data Management – Periodic Safety Update Reports for Marketed Drugs,ICH-E2D Post-Approval Safety Management – Definitions and Standards for Expedited Reporting, ICH-E2E Pharmacovigilance Planning
- **Pharmacovigilance regulations and guidelines**: Role of Pharmacovigilance in Drug Regulation, Regulatory aspects in Pharmacovigilance, European Union PV guidelines, Australian PV guidelines, Good Pharmacovigilance practices (GPP), Expedited reporting requirements
- **Pharmacovigilance in India:** Pharmacovigilance centers in India, CDSCO Indian PV guidelines-National Pharmacovigilance Program (NPP)
- **Pharmacovigilance in Europe:** Guidelines for Marketing Authorization Holders (MAH), General Principles, Risk management plan(RMP), Contents of EU-RMP, Expedited Reports, Reporting in Special Situations, Periodic Safety Update Report (PSUR)
- **Adverse Event reporting form**: MEDWATCH, CDSCO Adverse Event Reporting Form, CIOMS form for Serious Adverse event reporting, Anonymised Single Patient reports (ASPR-MHRA), Medication errors reporting

- **Pharmacovigilance Dictionaries**: MedDRA (Medical Dictionary for Regulatory Activities), MedDRA structure and content, WHOART (WHO-Adverse Reaction Terminology), Eudravigilance, CO-START
- **Global Pharmacovigilance & safety standards**- Pharmacovigilance activity in USA, Australia, WHO Monitoring of safety aspects – Uppasla Monitoring Center
- **Periodic safety update reports(PSUR) for marketed drugs :** Brief Introduction and Purpose of Periodic safety Update Report, PSUR Content, PSUR Process, Various Regulatory Requirement for PSUR

REFERENCES FOR READING

- A Handbook of Bioanalysis and Drug Metabolism by Gary Evans
- Biostatistics: The Bare Essentials by Norman G
- Clinical trial risk management by Martin Robinson & Simon Cook
- Clinical Trials: A Practical Guide to Design, Analysis & Reporting by Duolao Wang & Ameet Bakhai
- Data Monitoring committees in Clinical Trials Ebook by Susan S Ellenberg, Thomas R Flemming, David L Demets
- Drug Safety Evaluation by Shayne C Gad
- Guideline for Drug Regulatory Submissions by Sandy Weiberg
- Handbook of Bioequivalence testing by Sarfaraz K. Niazi
- Introduction to Statistics in Pharmaceutical Clinical Trials by Todd A Durham & J Rick Turner
- Phramaceutical statistics; Practical and Clinical Application by Sanford Bolton
- Practical Guide to - Clinical Data Management by Sisanne Prouscha
- The Design for studies for Medical Research by David Machin & Michael Campbell

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PRACTICAL EXERCISES & EXPOSURE

- Case studies solutions
- Technical and soft skill presentations
- Term search
- Development of Clinical research documents
    - SOPs development
    - CRFs & ICFs Preparation
    - Dummy clinical research and bioequivalence protocols etc,
- Role plays of real clinical research stake holders like Clinical research associate, investigator, project manager, volunteer, clinical research coordinator, auditor etc
- Technical article discussions
- Open book exam
- Mock exams
- Group Discussions

INDUSTRIAL EXPOSURE

During initial visit an overview of the facility infrastructure, flow of activity, visiting different areas like screening room, medical examination room, phlebotomy room, dining area, baggage and body area, clinical pharmacological unit, dosing area, investigator`s cabin, drug store, plasma separation and storage room.

On site exposure which includes observation of actual in-process activities like blood collection, plasma separation, screening of volunteers, informed consent process.

A visit to Analytical Department and Central Laboratory to have know-how of the tests/investigations conducted and other procedures performed in respective departments

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SEMESTER IV

DISSERTATION

- This crucial part of course gives you the chance to apply the research skills acquired during the taught phase of course to a practical problem in clinical research. The project can be undertaken in a variety of settings including academia or industry.
- This is a fantastic opportunity to apply your new found knowledge and skills in a real life setting; it also allows you to make invaluable contacts with potential employers before even completing the program. Also, working in a team, using knowledge and skills gained during the taught modules you will prepare a substantial platform for yourself to carry out diverse documentation activities at your end

- The marks are obtained from a combination of a submitted dissertation, oral presentation of your research and applications and initiative shown during the project