Pre-Clinical, Clinical Trial and Data Management

Sl. No.	Sub Code	Title	Teaching Dept.	Teaching hours/week			Examination				Credits
				L	T	P	Duration (Hrs.)	C.I.E. Marks	End Exam Marks	Total Marks	
		Theory subjects									
1	PCDM001	**Preclinical**		3	---		40	50	50	100	
2	PCDM 02	**CDM and Site Management**		4	---		40	50	50	100	
3	PCDM 003	**Biostatistics in Clinical Studies**		3	---		40	50	50	100	
4	PCDM 004	**Clinical writing**		3	---		40	50	50	100	
		Laboratory practice									
5	PCDML001	**Part A Preclinical and Data entry** **Part B Analytical methods and Medical writing**				8	80+80	50	50	100	
6	PCDML002	**Clinical Statistics**				8	160	50	50	100	
		Total		13		16					

Module1 Principle and Practice of Clinical Research and Pre Clinical Studies 40hours

Preclinical:

Guidelines for Research, Human and animal studies (Anatomy and Physiology),Pre-clinical trials : Definition, Types and Scope of Clinical Research, Good Clinical Practices, Drug Development Process, Careers in Clinical Research, Drug Discovery Process, Pharmacodynamics & Pharmacokinetics, Ethics in Clinical Research, Toxicity studies in animals, Special Clinical Trials, Medical Devices Trials, Scientific Integrity, Data acquisition, sharing and ownership,Publication practices and authorship

Historical Perspective on Clinical research

The earliest clinical research, The Greek and Roman Influence, Middle ages and Renaissance, Seventeenth, Nineteenth Century and Twentieth century and beyond, Legal issues, Clinical research and the media, Unanticipated risk in clinical research.Dichotomous response variables (two independent samples, paired dichotomous response, Sample size for continuous response variables (two independent samples) Sample size for repeated measures Sample size for equivalency of interventional studies Estimating sample size parameters

Clinical Research: Introduction to Clinical Trials: scope of clinical trial, clinical trials Phases, Phase I studies; Phase II studies; Phase III/IV studies Introduction to ethics of Clinical Trials. Clinical Trial Design, BA & BE Studies, Clinical Trial Development : Investigator Brochure, Informed Consent Form, Sponsor Monitor & Investigator responsibility, SOP in Clinical Trials,Clinical Trial Monitoring, Role of CRA, QA and QC in Clinical Trials, CRF Design,Clinical Trial Site Management, Pharmacovigilance

Study Population: Definition of study population, Issues on generalization. Practical aspects: recruitment (case method example) .Selection of the Questions: Primary question, Secondary question, adverse effects, Ancillary questions,

Study Design: Natural history, frequent errors. Basic Study Design observational studies, Randomized control studies, nonrandomized concurrent control studies, historical controls/databases, cross-over designs, factorial design, studies of equivalence, large clinical trials. The Randomization Process: Fixed allocation, randomization, simple randomization, blocked randomization, stratified randomization, Adaptive Randomization Procedures (baseline adaptive randomization procedures) Mechanisms of randomization. Blindness: Type of Trials – unblinded trials, Single Blind Trials, Double-blind Trials, Triple blind trials, Special problems in double blind studies – matching of drugs, coding of drugs and assessment of blindness.

Regulatory Affairs:

Historical Perspective, Ethical Issues, ICH GCP Guidelines, Schedule Y, ICMR guidelines for biomedical research, Regulatory Issues in US & Europe, Regulatory Issues in India,

Reference Books

- Management of data in clinical trials by by Eleanor McFadden
- A manager's guide to the design and conduct of clinical trials by Phillip I. Good

Module2: CDM and Site Management **40 hours**

Assessments, Data Collection and Reporting: Recruitment of Study Participants: strategies and Sources, monitoring, problems, reasons for participation, reducing dropout rates. Participant Adherence: Considerations before participant enrolment, maintaining good participant adherence, adherence monitoring, special populations. Assessing and Reporting Adverse Events: determinants of adverse effects (length of follow-up, frequency of events and individual susceptibility) reporting adverse events. Data collection and quality control: problems in data collection (major problems),minimizing poor quality data, training, pre-testing, techniques to reduce variability, data entry, quality monitoring. Design and Analysis of Surveys: instrument design, design of survey administration, sample design, data collection, analysis. Study Designs: Overview of Study Design: observational studies, experimental studies – uncontrolled studies, experimental studies – RCTs, other designs – equivalence, non-inferiority studies. Observational Studies: basic designs of observational studies, retrospective studies or cohort studies, sample size, bias and confounding, control of bias, control of the phenomenon of confounding. Experimental Design - issues of uncontrolled studies: before and after comparison in a single group, temporal variation of disease, temporal variation of the staff, equipment and environment, statistical regression to mean, learning effect, psychological effect. Confounders in observational studies: using the method of propensity score: the issue of confounders in observational studies, methods to control for confounders, the method of propensity score. Other designs: equivalence and non-inferiority studies, interim analyses, adaptive (flexible) design, studies with repeated measurements. Experimental Design – Randomized Clinical Trials: parallel-group design, stratified parallel group design, parallel group randomized block design, complete cross-over design, simultaneous treatments design, factorial design.

Clinical Research Site Management (Hospital Related)

Preparation of protocol, Audits & Inspection of Trial sites, Budgeting of Clinical trials, Multicentric Clinical Trials

Data Presentation, Analyses & Study Management: Data Capture: Optical Mark Recognition, electronic data capture, Optical Character Recognition; Data Presentation: Descriptive statistics, statistical hypothesis testing, denormalized; Handling missing data: imputations and challenges, adjusting for baseline variables, Methodological issues; Secondary analysis: Secondary analyses of the primary outcome, Secondary outcomes, Sub-group analyses: Uses and abuses, Bias in Randomized Controlled Trials; Study management: Monitoring process, Coordinating protocol implementation, Internal & external reporting; Performance Measures: timesheet, clinical monitor, Clinical Trial Management. Quality Assurance and Clinical Data Management and Monitoring Database audits, QA group, clinical monitoring, Clinical Trials Database; Reengineering the Clinical Data Management Process: formal methods, big bang, HMOs; Data Validation: data integrity, edit checks, Drug development; Ethical considerations, Adverse event coding and reporting, Role and responsibilities of the PI, Sponsor, Case Studies: Presentation of students protocols; Working with Contract Research Organizations: disaster recovery plan, CRO staff, CRO’s, CRFs, pharmaceutical industry.

2. Clinical Data Management and Oracle Clinical

Data planning, Designing, Data Capture, Data review, Reporting, OPEN CLINICA 2.0:Understanding Protocol, Understanding SOP, Objects in Open Clinica, Overview of Study setup, Setup a program & project, Study configuration & Study design, Setup plan events & Informed consent form, Investigator, Site & patient positions, Manage Treatments, Define DCM, DCI, CRF designing, Validation, Derivation Process, Entering CRF data, Discrepancy Management, Submission Process.

Reference Books :

- Clinician's Guide to Medical Writing By Robert B Taylor
- Understanding Oracle Clinical by Safari Books online
- Oracle® Clinical by Oracle® Clinical Release Notes

Module 3: ***Biostatistics in Clinical Studies*** **40 hours**

Basics: data classification, data distribution, descriptive methods for categorical data, descriptive methods for continuous data. Statistical Tests (note: only basics of statistical tests will be covered), estimation of parameters, comparison of population, proportions, comparison of population means, correlation and regression. Sample Size: dichotomous response variables (two independent samples, paired dichotomous response).Sample size for continuous response variables (two independent samples).Sample size for repeated measures, Sample size for equivalency of interventional studies, Estimating sample size parameters. Survival Analysis: Estimation of the survival curve (Kaplan Meier estimate).Comparison of two survival curves, covariate adjusted analysis, use of survival analysis in clinical research. Other Issues in Data Analysis 1:Poor quality or missing data, Intention-to-treat analysis, Competing events, Covariate adjustment. Other Issues in Data Analysis 2: subgroup analyses, comparison of multiple variables, use of cut points, meta-analysis of multiple studies. Probability and Normal Distributions, Estimation, Hypothesis Testing, ANOVA ,

Statistics for clinical trials

Types of data in clinical trials, Computer System Validation**:** 21 CFR 11, CTM system, Introduction to CDISC, GCDMP, Data Management Plan, CRF designing, DB designing & CRF Annotations; Systems Software Validation Issues: auto encoder, User Acceptance Test, SDLC; Oracle Clinical, workflow, Intelligent Character Recognition; Basic Clinical Research tools and Resources for Data Management and Analysis SAS CLINICAL: Introduction to SAS in CDM , components of SAS, Different data types, Base/SAS, SAS/STAT, SAS/GRAPH, SAS/ACCESS, SAS Procedures, SAS Macros, Brief Introduction to SQL, SAS/SQL, SAS Enterprise Guide 4.1

TLG(Tables listings and Graphs) of clinical trials in SAS, Tables in clinical trials, Screening failures, Subject disposition, Subject disposition by visits, Premature discontinuation from study medication, Subject disposition by center, Protocol deviation, Demographics and baseline characteristics, Medical and surgical history, Gynecological history, Screening Pap smear, mammography and serum pregnancy test results

Listings : Listing of Hematological parameters with low and high flags, Listing of blood chemistry with low and high flags, Subject listings for adverse events /serious adverse events, Subjects with death information.

Figures : Bar chart of change in Diastolic and systolic blood pressure at final visit, Bar chart of urine drug concentration post dose collections 0 to 72 hours in Pharmacokinetics studies(standard deviation plotted over vertical bars using annotation data sets in SAS, Plot of systolic blood pressure 0 to 24 hours after dosing of study drug, Plots of plasma drug concentration0 to 72 hours in Pharmacokinetics studies(mean and standard deviation plotted at each point using annotation data sets in SAS., Kaplan Meire survival curve, Power curve for study design sample size.

Reference Books

- Fundamentals of clinical trials by Lawrence M. Friedman, Curt Furberg, David L. DeMets
- Practical Guide to Clinical Data Management, Second Edition by Susanne Prokscha

Module 4: Clinical writing 40 hours

Technical Writing

Technical Issues in Medical Writing, Publication writing, Regulatory writing, Safety Writing, Medico-Marketing Writing, Oral Presentation and Communication Skills

Medical Coding

Introduction, Physiology and Anatomical Coding, Professional guidelines for medical coding : ICD -International Classification of diseases, CPT -Current Procedural terminology

Reference Books

- *support.sas.com/documentation/onlinedoc/91pdf*
- Professional SAS Programmer's Pocket Reference by Rick Aster
- Professional guide for medical coding
  1. ICD -International Classification of diseases
  2. CPT -Current Procedural terminology

Practicals

Lab I

Part A Preclinical and Data entry 80 hours

1. Planning a clinical study in Oracle Clinical
2. Designing a study
3. Designing Case Report Forms (CRFs) in Oracle Clinical
4. Testing Data Entry Forms and performing Test Data Entry
5. Designing Validation and Derivation Procedures in Oracle Clinical
6. Production data entry in Oracle Clinical
7. Discrepancy management in Oracle Clinical
8. DCF Management, Printing and Maintenance in Oracle Clinical
9. Animal Handling
10. Routes of administration of Drugs

Part B Analytical methods and Medical writing 80 hours

Analytical techniques: 30 hours

1. Chromatographic techniques
2. Spectroscopic techniques
3. Electrophoretic techniques
4. Stereoscopic techniques,
5. Cytometry & Flurometry
6. Thermal methods of analysis

Medical writing: 50 hours

1. Introduction to effective medical writing
2. Technical writing for pharmaceutical , medical device and biotech industries
3. Writing effective standard operating procedures and other process documents
4. Electronic common technical document
5. Preparation of FDA submissions and communicating with FDA

LabII Clinical Statistics 160 hours

1. Introduction to SAS
2. Running SAS programs
3. Descriptive information and statistics
4. An overview of statistical tests in SAS
5. Exploring data with graphics
6. Using where with SAS procedures
7. Missing values in SAS
8. Common SAS options
9. Overview of SAS syntax of SAS procedures
10. Common error messages in SAS
11. Inputting raw data into SAS
12. Reading dates into SAS and using date variables
13. Creating and recoding variables
14. Using SAS functions for making/recoding variables
15. Subsetting variables and observations
16. Labeling data, variables and values
17. Using Proc Sort and the BY statement
18. SAS Functions