Swami Ramanand Teerth Marathwada University, Nanded

Syllabus M.Sc Clinical Research (Revised)

Choice Base Credit System (CBCS) June-2014

Objectives of the course:

This course is with the following objectives –

• To provide the students with the requisite knowledge that will enable them to pursue a career in the Clinical Research industry.

• Synthesize the highest academic standards with relevance to the need to present business & commercial policies.

• Encourage clinical research methodologies & start PhD programs in clinical research.

• Collaborate with organizations at national & international level in areas of research, training, seminars & conferences.

•Represent the interest of clinical research professionals in the country & ensure that India does not lag behind in maintaining the internationally prescribed standards of clinical Ethics.

• To give students in-depth training in both the theoretical and practical aspects of clinical research, regulatory affairs and clinical data management in the clinical research industry.

Eligibility

• Graduate or post graduate from a recognized university in Life Sciences (Biochemistry, Pharmacology, Toxicology, Biotechnology, Microbiology, Botany or Zoology)

• Graduates of Medical Sciences (MBBS/ BDS/ BAMS/ BHMS/ BUMS/ BVSc/BSSM)

• Bachelors in physiotherapy, pharmacists (B.pharm, M.Pharm)

• Nursing graduate.

First Semester :

Paper No.	Paper Title	External (ESE)	Internal (CA)	Total
CRT-101	Fundamentals of clinical operations	(75 marks)	(25 marks) (2Test : 15 marks+ 1Assignment:10 marks)	Credit: 4 (100 marks)
CRT-102	Clinical Data Management	(75 marks)	(25 marks) (2Test : 15 marks+ 1Assignment:10 marks)	Credit: 4 (100 marks)
CRT-103	Statistics for Clinical Research	(75 marks)	(25 marks) (2Test : 15 marks+1Assignment :10 marks)	Credit: 4 (100 marks)
CRT-104 Elective)	Basics of Pharmacy, Drug discovery & development.	(75 marks)	(25 marks) (2Test : 15 marks+ 1Assignment:10 marks)	Credit: 4 (100 marks)
CRT-105	Seminar	25Marks		Credit: 1
			Total for Sem: I	**Credit: 17**

Second Semester:

Paper No.	Paper Title	External (ESE)	Internal (CA)	Total
CRT-201	IPR & Data Exclusivity, Bioethics in Clinical Research	(75 marks)	(25 marks) (2Test : 15 marks+ 1Assignment :10 marks)	Credit: 4 (100 marks)
CRT-202	Pre Clinical Studies	(75 marks)	(25 marks) (2Test : 15 marks+ 1Assignment:10 marks)	Credit: 4 (100 marks)
CRT-203	Pharmaceutical Biotechnology	(75 marks)	(25 marks) (2Test : 15 marks+1Assignment:10 marks)	Credit: 4 (100 marks)
CRT-204 Elective)	Basics of Molecular Biology & Biotechnology	(75 marks)	(25 marks) (2Test : 15 marks+ 1Assignment:10 marks)	Credit: 4 (100 marks)
CRT-205	Seminar	25Marks		Credit: 1
			Total for Sem: I I	**Credit: 17**

Detailed syllabus:

First Semester :

CRT-101 Fundamentals of Clinical Operations. Hours : 45

Unit 1: Introduction to Clinical pharmacology, Overview of Clinical Research Process Drugs.

Drugs: Acting on Nervous System, Drugs Acting on Respiratory System, Drugs Acting on Gastrointestinal System, Drugs Acting on Cardiovascular System, Drugs Acting on Kidney, Autacoids and Related Drugs, Hormones and Related Drugs, Drugs Affecting Blood and Blood Formation, Antimicrobial Drugs, Anticancer Drugs.

Unit 2: Medical terminologies and Clinical Research terminologies:

Medical Terminologies, List of Symbols/Abbreviations, Abbreviations/Terminologies, Clinical Research Terminologies, Glossary of Clinical Trials Terms.

Unit 3: Phases and Types of Clinical Trials & Good Clinical Practice, GCP-FDA, GCP-WHO :

Introduction to Clinical trials, Phases of Clinical Trials, Types of Clinical Trials, Randomized Clinical Trial, Non Experimental clinical trials, Superiority trials. Introduction to Clinical trials, Phases of Clinical Trials, Types of Clinical Trials,Randomized Clinical Trial, Non Experimental clinical trials, Superiority trials.

Unit 4: Site selection, site initiation, monitoring and site closeout:

Site Selection Visit: Introduction to Site Selection Visit, Flow of Events Prior to SSV, Feasibility Study, SSV Checklist, On Site visit, Elements of Discussion during the SSV, Documentation and Reporting. Site initiation Visit : Introduction, Trials, Initiating the Study, Site initiation process, Procedure Site Monitoring and Site Close Out: Monitor, Responsibility of the Monitor, Aims of Monitoring, Monitoring Plan, Preparation for Monitoring Visits, Monitoring activities, Documenting the Monitoring Visit, Follow-up of Persistent Non-Compliance at site, Site Close Out, Flow of Events Prior to Site Close Out Visit, On Site Close Out visit

CRT-102 Clinical Data Management **Hours : 45**

Unit 1: Introduction to Clinical Data Management and SOPs
Introduction to CDM, Computer system validation (CSV), Clinical Data Management flow, Data Management team, Roles and responsibilities of key team members and sponsor, SOPs of data management, review and authorization. CRF design , Procedure for CRF design, elements of CRF,data points to be captured in individual CRFs. Database design and build ,Introduction to data basedesign and build, data base design, data base validation. Clinical data entry process ,Data entry screenvalidation, data entry process, symbols, data entering.

Unit 2: Electronic data and lab data loading ,Electronic data interchange-Architecture for EDI, Advantages of using EDI, barriers to implementation, positives and negatives ,Lab data loading -Roles and responsibilities of lab loader technician, helpdesk, study coordinator,
-loading lab data, electronic/lab file contents, typical problems, lab data findings, Quality Assurance,SOPs for processing lab data, taking lab data seriously.

Unit 3: Quality control of clinical data ,Terminology and definitions, quality control process, data errors and quality measurement, responsibilities, operational QC, data management matrix

Unit 4: Database lock and data transfer ,Introduction to data base lock, minimum standards, procedure, errors found after database closure, freezing the data base, best practices, recommended Standard Operating Procedures. Introduction to data transfer, procedure, best practices

CRT-103. Statistics for Clinical Research **Hours : 45**

Unit 1: Introduction and basic concepts ,Overview of the drug development process, bias, randomization, blinding, choice of control group. Organization and display of data, Types of data, graphical diagrammatic representation of data.

Unit 2: Measures of Central tendency ,Mean, median, mode, measure of dispersion ,Standard Deviation, Standard Error, Variance, range, Coefficient of Variation. Skewness & Kurtosis, important considerations

Unit 3: Correlation and Regression
Correlation: - Research question, types of data required, assumptions, correlation coefficient, significance of correlation, meaningfulness of correlation coefficient
Regression :- Research question, types of data required, assumptions, simple linear regression.

Unit 4: Probability and probability distributions, Definitions, probability distribution curves. Continuous probability distribution-Normal distribution, properties and applications. Discrete probability distribution-Binomial & Poisson distribution, properties and applications. Test of significance-F –test, t-test & chi-square test. Statistical input during protocol design, Demonstration of sample size calculation: comparing two means, Sample size computation for bioequivalence tests.

CRT-104 (Elective) Basics of Pharmacy, Drug discovery & development.

Hours : 45

Unit 1: History of Pharmacy, Indian Pharmaceutical industry, Drugs-sources, nomenclature, classification, Pharmacopoeias, Formulary, Codex. Branches of Pharmacy: Pharmacognosy, Pharmaceutical chemistry, Quality Assurance, Pharmaceutics, Pharmacology, Pharmacy Management and Pharmacy Practice. Pharmaceutical Manufacturing-Quality Assurance and Quality Control

Unit 2 : Drug Regulatory Environment-Pharmaceutical Legislation in India, Drug regulatory authorities, International Conference on Harmonization, Good Practices and Quality Management, Drug Master File

Unit-3 : Drug Discovery & Development. History of drug development, Drug Discovery Pipeline, Drug Discovery Process. Approaches to Drug Discovery: Synthetic/medicinal chemistry, combinatorial synthesis, Natural Product, In Silico approach or CADD, QSAR, Discovery Genomics

Unit-4 : Personalized medicines, High throughput screening. Manufacturing and packaging ,Manufacturing-Multitasking machines Packaging- cGMP, USP requirements on containers and closures, Quality Control, Inhalation drug products, drug products for injection, drug products for ophthalmics, liquid based oral and topical drug products, post approval packaging changes

Second Semester:

CRT-201 IPR & Data Exclusivity, Bioethics in Clinical Research
Hours:45

Unit 1: Intellectual property rights, Laws of IPR, patents, The World Trade Organization and the TRIPS agreement, copy rights, the rationale for IP protection, the evidence about the impact of IP, Technology Transfer, Contracts and Agreements

Unit-2: The Data Protection Act & data mining, data and disclosure, data exclusivity, data exclusivity as a governmental function, commercial and economical rationale for test data, confidentiality, current state of data protection.

Unit-3: Introduction to bioethics, ethical issues in preclinical (animal) studies, & clinical studies-Ethical principles, Institutional Review Board, Special issues in research. Ethical Guidelines-ICMR, Institutional Ethics Committees, Institutional Review Board, Ethics-SOPs Ethical issues based on methodology of clinical Research. The ethics of clinical research in developing countries.

Unit-4: Basic philosophies of animal ethics: (3 'R's), Animal Ethics Committee, executive, meetings, confidentiality and indemnity, period of approval, joint animal ethics committee, process to establish an AEC, guidelines for ethical conduct in the care and use of animals. Social responsibility for clinical researcher.

CRT-202 Pre Clinical Studies & safety Hours:45

Unit 1: Experimental animals used, Equipments used in ATC, Sterilization techniques, media for animal cell culture. Cell culture and cell lines, concepts in mammalian and non-mammalian culture, applications of cell culture.

Unit-II: History of toxicity, relationship between dose and toxicity, types of toxicity, factors influencing toxicity, toxins, toxicity studies, special toxicity studies, in vitro models, in situ methods, in vivo models.

Unit III: Good Laboratory Practices, ICMR-GLP guidelines, FDA-GLP guidelines, Organization and personnel, facilities, equipment, testing facilities operation, test and control articles, protocol for and conduct of a non-clinical laboratory study, records and reports, disqualification of testing facilities, OECD-GLP guidelines, quality assurance program, facilities, test systems, test and reference items, Standard Operating Procedures, Performance of the study, reporting of study results, storage and retention of records and materials.

Unit-IV: Drug action, mechanism of drug action, dose-response relationship, therapeutic index, undesirable effects, disease modeling–hypertension, asthma, acidity, arthritis, cancer, addiction, autoimmune diseases, pain, epilepsy, inflammation

CRT-203 Pharmaceutical Biotechnology Hours:45

Unit I: introduction to pharmaceuticals - History and Development Introduction to Biotechnology-An Introduction, History of Biotechnology, Applications of Biotechnology, Pharmaceutical Biotechnology, Developments in use of biopharmaceuticals

Unit II: History of fermentation, Fermentation Technology, types of Fermenters, Fermentation kinetics, fermentation process, Product Recovery or Down stream processing,

Unit III : History of vaccine, Immunization, Types of Vaccines, Manufacture of Vaccines, An Overview of technology in Vaccine Development, recombinant vaccines, New vaccines under trial. History of monoclonal antibodies, Immunity and antibodies, Hybridoma technology, Production of monoclonal antibodies, Applications of Monoclonal Antibodies

Unit IV: Blood products-Whole blood and its components, Common products made from blood and their uses. Enzymes-Sources and production of enzymes, Uses of enzymes, Important therapeutic and other medical / pharmaceutical uses of enzymes. Proteins-Production of Lowcomplexity
Proteins, Production of Complex Proteins, Therapeutic proteins Recombinant
Products-Production of recombinant products, Selected recombinant proteins

CRT-204 Basics of Molecular Biology & Biotechnology

Hours:45

Unit I: Major events in Genetics history, Nucleic acid, Structure of Nucleic acid, Chemistry of Nucleic acid, DNA replication and repair, mechanism of replication, Origin of replication, Process of replication, Completion of replication

Unit II: Transcription, RNA polymerase, mechanism of transcription in prokaryotes & eukaryotes, Initiation, Elongation, Termination of transcription. Post Transcriptional modifications:5' end capping, Poly A tail, RNA splicing, the chemistry of primary RNA transcript splicing. Translation: Genetic code, Translation process, Stepwise formation of polypeptides on ribosome's. post translation modification of proteins.

Unit III: Gene regulation, Jacques Monad's early experiments, The Operon model for gene expression, operon concept, the lactose operon, tryptophan & arabinose operon.Role of cAMP & CRP in lac operon.

Unit IV: Recombinant DNA technology, DNA sequencing, Cell and Tissue culture, Extraction, Separation, PCR, RFLP, Micro arrays, animal tissue culture, Tissue culture methods, Tissue culture practices, Polymerase chain reaction, Molecular diagnostics.

CRP-I : Lab Course-I

1. Determination of absorption maxima for identification & confirmation of different antibiotics.
2. Bioassay of different antibiotics
3. Determination of MIC using different pharmaceuticals.
4. Sterility testing of different pharmaceuticals.
5. Determination of microbial resistance to various antibiotics.
6. Determination of antimicrobial activity of disinfectants.
7. Microbial limit tests (MLT)

CRP-II : Lab Course-II

1. Collection of data & statistical calculations
2. Preparation of charts/graphs
3. Problems based on measure of central tendency.
4. Problems based on measure of dispersion.
5. Problems based on test of significance-t-test, F-test, chi-square test.
6. Problems based on correlation & regression.
7. Problems based on Probability.

Lab-Course-III

1. Media formulation & optimization
2. study of growth kinetics of microorganisms by turbidometry & SCP.
3. Determination of growth curve of microorganism & determination of substrate degradation profile.
4. Study of scale up of fermenter.
5. Microbial production of antibiotics(penicillin, streptomycin etc.)
6. Use of alginate for cell & enzyme immobilization.
7. Testing of antibiotic resistance among isolates of bacteria from nature.
8. Microbial production of enzymes & its downstream processing.
9. Microbial production of recombinant proteins & separation by HPLC,FPLC etc.
10. Industrial visit.

Lab-Course-IV

1. Isolation of DNA from bacteria & animal cells.
2. Agarose gel electrophoresis by using DNA markers for molecular Wt. determination.
3. Study of in vitro transcription & translation.
4. RFLP.
5. PCR
6. Southern blotting
7. Western blotting
8. Northern blotting
9. Culturing of anchorage dependent & independent animal cells.
10. MTT assay for cell viability & growth.
11. Cell fusion with PEG

Reference Books :

01 Pharmacology and Pharmacotherapeutics Satoskar,18th ed, 2003
02 An introduction to Biostatistics PSS Sundar Rao, G Jesudian, J Richard
03 Preventive and Social Medicine Banarasidas Bhanot, Jabalpur, India.19th Edition
04 Public Health and Preventive Medicine Appleton and Lange, California
05 Basic and Clinical Pharmacology Bertrand Katzung
06 Essentials of Medical Pharmacology K. D Tripathi
07 Pharmacology Rang, Dale and Ritter
08 Gene Silencing by RNA Interference Muhammad Sohail
09 Biochemistry Stryer
10 Biochemistry Lehninger, Nelson
11 Developmental Biology Gilbert
12 Molecular Biology of the Cell Alberts
13 Animal Cell Culture and Tech Butler
14 Molecular Cell biology Lodish
15 Gene VIII Lewin
16 Handbook of Stem Cells Lanza -2nd Ed
17 Molecular Cloning Sambrook, 3rd Ed-3 volumes
18 Principles and Techniques of Biochemistryand Molecular Biology Wilson
19 Basic Cell Culture protocol Pollard
20 Cody, R. Cody's Data Cleaning Techniques using SAS SoftwareCary, NC: SAS Institute Inc;
21 Intellectual Property Rights Narayanan P, 3rd Ed. Eastern Law House.
22 Drug discovery and development Bhushan Patwardhan
23 Clinician's Guide to Medical Writing Robert B. Taylor. 1st ed. 2004. Springer

.

Swami Ramanand Teerth Marathwada University, Nanded

Syllabus M.Sc Clinical Research (Revised)

Choice Base Credit System (CBCS) June-2014

Skeleton for Theory Paper

……

Time-3 hours. Maximum Marks-75. Credits-3

……

Note-1. Attempt all questions.
2. All questions carry equal Marks.
3. Draw neat and labeled diagram wherever necessary.

Q.1 Long answer type question (Based on Unit I) …….15

OR

a) Short answer type question (Based on Unit I) ……..…08
b) Short answer type question (Based on Unit I) ……..07

Q.2 Long answer type question (Based on Unit II) …….15

OR

a) Short answer type question (Based on Unit II) …….08
b) Short answer type question (Based on Unit II) …….07

Q.3 Long answer type question (Based on Unit III) …….15

OR

a) Short answer type question (Based on Unit III) ……08
b) Short answer type question (Based on Unit III) ……07

Q.4 Long answer type question (Based on Unit IV) …….15

OR

a) Short answer type question (Based on Unit IV) ……08
b) Short answer type question (Based on Unit IV) ……07

Q.5 Write short note on any three of the following……15

1. Based on unit –I 2. Based on unit –II 3. Based on unit –III 4. Based on unit –IV

5. Based on unit –I/II/III/IV.