MGM INSTITUTE OF HEALTH SCIENCES

(Deemed to be University u/s 3 of UGC Act, 1956)
Grade 'A++' Accredited by NAAC
Sector-01, Kamothe, Navi Mumbai -410 209
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Curriculum for

Fellowship in Clinical Research

(with effect from 2022-23 Batches)

Approved as per AC -44/2022, Dated 09/12/2022

Amended History

1. Approved as per AC -44/2022 [Resolution No.5.29], Dated 09/12/2022.

Annexure-32 of AC-44/2022

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Fellowship in Clinical Research
(FCR)
One year full time course
(Two semesters)

Fellowship in clinical Research (Semester-I and II)

General Rules

O.1 A candidate for fellowship in clinical research must possess the basic degree in science of this university or any other university recognized by this university (graduates from multidiscipline like MBBS / B.D.S / B.A.M.S / B.H.M.S /B. Pharmacy / BVSC/ B.Sc.(Life sciences) / B.Pharm / B. Physiotherapy etc)

(The eligibility criterion for selection is minimum 50% of marks in the university examination in basic degree in multidisciplinary sciences mentioned above)

O.2 Fellowship in clinical research semester I and II examinations will be held at the end of each semester and remedial examination will be held during the middle in each semester.

O.3 Candidates for fellowship in clinical research (semester-I and II) examination shall be examined after they have satisfactorily completed the prescribed courses of study

. O.4 Regular records of lectures and tests, conducted at the institution, imparting training for this course, shall be maintained for each student and minimum 75 % of attendance is mandatory.

O.5The syllabus laid down for various papers of fellowship in clinical research (semester-I and II) examination is attached separately at the end of the rules.

O.6 No class shall be awarded to the successful candidate at the fellowship in clinical research (semester-I) examination.

O.7It is essential to attend seminar/conferences/training/visit of premier hospitals/industry visit in the area of dialysis or other relevant areas.

At the end of First semester, the student has to undertake clinical training at hospitals/clinic for minimum one month period

The summary of the work done in the clinics/hospitals must be submitted at the end of this clinical training.

- **Scope of the Subject:**
- This course aims to provide the students an opportunity to learn drug development process especially the phases of clinical trials and also the ethical issues involved in the conduct of clinical research.
- Also, it aims to imparts knowledge and develop skills on conceptualizing, designing, conducting and managing clinical trials.

- **Objectives of the study:**

  Upon completion of this course it is expected that students shall be able to:
- Know the new drug development process.
- Understand the regulatory and ethical requirements.
- Appreciate and conduct the clinical trials activities
- Know safety monitoring and reporting in clinical trials
- Manage the trial coordination process

Syllabus for Diploma in Clinical Research

1. **Fundamentals of Clinical Research**
2. **Drug Discovery and Development including BA/BE Studies**
3. **Clinical Research Methodology and Pharmacovigilance**
4. **Ethics and Regulations in Clinical Research**
5. **Clinical Trial Documentation**
6. **Clinical Data Management and Biostatistics**

I Semester

1. Fundamentals of Clinical Research

- **Course Objective:**
- To Introduce the students to the field of clinical research
- To make the student understand the importance of clinical research
- **Course Contents:**
- **Basic terminologies in Clinical Research**
- **Historical Perspectives**
- Nuremberg Code Study,
- The Belmont Report
- The declaration of Helsinki
- Origin and Principles of International Conference on Harmonization –GoodClinical Practice (ICH-GCP) guidelines

- **Informed Consent Process**
- Ethical principles governing informed consent process
- Structure and content of a Patient Information Sheet
- Structure and content of an Informed Consent Form
- The process of taking informed consent and documentation

- **Types and Designs used in Clinical Research**
- Types of research designs based on Controlling Method (Experimental, Quasi experimental, and Observational methods)
- Randomization techniques (Simple randomization, restricted randomization, blocking method and stratification),
- Time Sequences (Prospective and Retrospective),
- Sampling methods (Cohort study, case Control study and cross sectional study),
- Health outcome measures (Clinical & Physiological, Humanistic and economic)

- **Clinical Trial Study team**
- Roles and responsibilities of: Investigator, Study Coordinator, Sponsor, Monitor, Contract Research Organization, Site management Organizations.

- **Text & References:**
- Text: • Basic Principles of Clinical Research and Methodology by S.K.Gupta
- Central Drugs Standard Control Organization. Good Clinical Practices-Guidelines for Clinical Trials on Pharmaceutical Products in India. New Delhi: Ministry of Health; 2001.
- International Conference on Harmonization of Technical requirements for registration of Pharmaceuticals for human use. ICH Harmonized Tripartite Guideline. Guideline for Good Clinical Practice.E6; May 1996.
- Ethical Guidelines for Biomedical Research on Human Subjects 2000. Indian Council of Medical Research, New Delhi.
- Principles of Clinical Research edited by Giovanna di Ignazio, Di Giovanna and Haynes.
- Deborah Rosenbaum, Michelle Dresser. Clinical Research Coordinator Handbook Second Edition
- Practical Clinical Trials Series GCP Tools and Techniques Interpharm/CRC New York Washington, D.C.© 2002
- Duolao Wang and AmeetBakhai Clinical Trials A Practical Guide to Design, Analysis, and Reporting. Remedica 2006

- **Practical:**
- Visit to hospital
- General examination of the patients
- Introduction to various instruments used in clinical research
- Training about various sample collections done in clinical research
- To prepare and submit Informed Consent Form (ICF) for dummy clinical data
- To prepare and submit dummy patient information sheet (PIS) for dummy clinical data
- To prepare protocol for dummy clinical data

2. Drug Discovery and Development including BA/BE Studies

- **Course Objective:**
- To enrich the student'sknowledgein the process of drug discovery and development in clinical trials.
- To know the importance of drug discovery and development in clinical research.
- **Course Contents:**

- **Introduction to Drug Discovery and Development**
- Basic pharmacology and clinical research:
- Basic conceptual knowledge about receptors, drugs, preclinical studies, pharmacodynamics, pharmacokinetics (ADME), drug interactions, clinical research,
- Clinical Pharmacokinetics and Pharmacodynamics
- Therapeutic drug monitoring

- **Clinical trials -New drug discovery process-**
- Purpose,
- Main steps involved in new drug discovery process,
- Timelines of each steps,
- Advantages and purposes of each steps,
- Pre clinical toxicology:
- General principles,
- Systemic toxicology (Single dose and repeat dose toxicity studies),
- Carcinogenicity, Mutagenicity, Teratogenicity, Reproductive toxicity, Local toxicity, Genotoxicity, animal toxicity requirements
- Phase-I, II, III, IV trials. –
- Introduction and designing -Various phases of clinical trials -Post Marketing surveillance – methods –
- Principles of sampling -Inclusion and exclusion criteria –
- Methods of allocation and randomization -Informed consent process in brief –
- Monitoring treatment outcome

- -Termination of trial
- -Safety monitoring in clinical trials
- **Bioavailability and Bioequivalence**
- TEXT BOOKS and REFERENCES:
- (1) Basic and Clinical Pharmacology, Prentice hall, International, Katzung, B.G.
- (2) Clinical pharmacokinetics, Pub. Springer Verlab, Dr. D.R Krishna, V. Klotz
- (3) Remington Pharmaceutical Sciences, Lippincott, Williams and Wilkins
- (4) Pharmacological Basis of Therapeutics-Goodman and Gilman
- (5) Text book of Biopharmaceutics, Dr. Brahmankar
- (6) Drug Discovery and Development , 2nd Edition by Raymond G Hill
- (7) Drugs: From Discovery to Approval by Rick Ng

- **Practical :**
- 1. To prepare and submit protocol for Phase I , Phase II ,Phase III & PMS Studies for the given dummy clinical data
- To calculate bioavailability of given drug by different methods.

3. Clinical Research Methodology & Pharmacovigilance

- **Course Objective:**
- To make the student understand the importance of Pharmacovigilance and Pharmacoepidemiology in clinical research

- **Course Contents:**
- **Pharmacovigilance**
- Introduction to Pharmacovigilance and safety monitoring
- a. Scope, definition and aims of Pharmacovigilance
- b. Adverse drug reactions - Classification, mechanism, predisposing factors, causality assessment [different scales used]

- c. Reporting, evaluation, monitoring, preventing & management of ADRs
- d. Global and IndianPharmacovigilance System
- Adverse drug reaction reporting and monitoring Drug induced diseases
- Medical Devices and Materiovigilance

- **Pre-Marketing Methodologies in Pharmacovigilance**
- **Post-Marketing Methodologies in Pharmacovigilance**
- Sources and Documentation of Individual Case Safety Reports (ICSRs)
- Medical dictionary (MedDRA) and Medical aspects in Pharmacovigilance
- Medical Information System
- Special cases in Pharmacovigilance
- Standard operating procedures in Pharmacovigilance

- .**Safety Monitoring in Clinical Trials:**
- Pharmacovigilance Database And Signal Detection Tools
- Risk –benefit assessment and management in Pharmacovigilance
- Compliance monitoring and Pharmacovigilance inspections Ethics Committee – Schedule Y
- **Pharmacovigilance communications**
- Case triage , Case entry , Case processing
- **Global regulatory requirements and guidelines in Pharmacovigilance**
- Regulatory submissions (E2b, MHRA, FDA)
- Periodic Safety Update Reports (PSUR,s) For Marketed Drugs (ICH E2C) Schedule Y - ICMR

- **Text books and References:**
- (1)International Conference on Harmonization of Technical requirements for registration of Pharmaceuticals for human use. ICH Harmonized Tripartite Guideline. Guideline for Good Clinical Practice.E6; May 1996.

- (2)Ethical Guidelines for Biomedical Research on Human Subjects 2000. Indian Council of Medical Research, New Delhi.
- (3)Textbook of Clinical Trials edited by David Machin, Simon Day and Sylvan Green, March 2005, John Wiley and Sons.
- (4) Ronald D. Mann, Elizabeth B. Andrews. Pharmacovigilance. John Wiley & Sons Ltd, 2002 (5) Guidance Document Pharmacovigilance Programme of India (PvPI)
- (6)Shayne C. Gad. Drug Safety Evaluation. A John Wiley & Sons, Inc., Publication
- (7)Guidance Document Materiovigilance Programme of India (MvPI) Version 1.2
- (8) Principles of Clinical Research edited by Giovanna di Ignazio, Di Giovanna and Haynes.
- (9) Assuring Data Quality And Validity In Clinical Trials For Regulatory Decision Making : Janet Woodcock, Frederick Ognibene, John Overbeke.2003;Welly Publication
- (10) Clinical Pharmacy and Therapeutics Roger walker and Clive Edwards,Churchill Livingstone Edinburgh

- **Practical:**
- To assess causality for the given case of ADR (Adverse Drug Reaction) and submit using the appropriate scale
- To assess Probability for the given dummy case of ADR (Adverse Drug Reaction) and submit using the appropriate scale
- To assess and submit Severity for the given dummy case of ADR
- To prepare and submit the Reporting of SAE(Using the appropriate forms)
- To prepare and submit SOP(Standard Operating Procedures) for ADR reporting

- **Clinical Research Methodology**
- Definitions: epidemiology, Disease distribution, disease determination, disease frequency,
- Aims of epidemiology, Difference between epidemiology and clinical medicines,
- Epidemiological approach,
- Measurements in epidemiology, (rates, ratios, and proportions)
- Measurement of morbidity: Incidence, Prevalence, uses of prevalence, relationship between incidence and prevalence

- Research Methodology
- a) Types of clinical study designs: Case studies, observational studies, interventional studies,
- b) Designing the methodology
- c) Sample size determination and Power of a study
- Determination of sample size for simple comparative experiments, determination of sample size to obtain a confidence interval of specified width, power of a study
- d) Report writing and presentation of data
- Epidemiological methods:
- (1) Descriptive epidemiology:
- (2) Analytical epidemiology:
- Case control study: Selection of cases, selection of controls, matching, measurements of exposure, analysis, odds ratio, bias in case control study., advantages, disadvantages and some examples of case control study
- Cohort study: Concept, framework, prospective and retrospective cohort study, combination of prospective and retrospective cohort study, elements of cohort study, relative risk, attributable risk, advantages, disadvantages and examples of cohort study.
- (3) Experimental epidemiology:
- Randomized controlled trials: Protocol, selecting reference and populations, randomization, manipulation, follow-ups, assessment, study designs in randomized trials like parallel and cross over study, Types of randomized controlled trials: clinical trial, preventive trials, risk factor trials, trial of etiological agents.
- **Pharmacoeconomics**

- **Practical:**

1. Introduction to Pharmacoepidemiology
2. Measurement of outcomes in PE
3. Concept of Risk in PE
4. Drug Utilization Review
5. Spontaneous Reporting System
6. Prescription event Monitoring
7. Pharmacoeconomics Evaluation

- **RECOMMENDED BOOKS:**
- Clinical Epidemiology, Brian Haynes, David L Sackett, 3rd edition,
- Quantitative Methods for Health Research, Nigel bruce, Daniel Pope

- **Suggested List of Practical Assignments**
- Students are expected to submit TWO written assignments (1500 – 2000 words) on the topics given to them covering the following areas dealt in theory class.
- 1. Assignments on Measurement of risk, attributable risk and relative risk, timerisk relationship and odds ratio with the help of examples
- 2. Assignments on study of various Pharmacoepidemiological parameters with the help of case studies for individual methods
- 3. Assignments on various Pharmacoeconomic outcome analysis with the help of case studies for individual methods (Four) Cost – minimization, cost- benefit, cost – effectiveness, cost utility methods

II Semester

4. Ethics and Regulations in Clinical Research

- **Course Objective:**
- To enrich the students' role and responsibility in clinical trial documentation in clinical trials by making them aware about ethical practices and various regulations
- To know the importance of ethics and regulations in clinical research.
- **Course Contents:**
- Introduction to Bioethics
- Good Clinical Practice: ICH guidelines Indian GCP guidelines (CDCSO guidelines)
- ICMR Guidelines - Ethical Guidelines for Biomedical Research on Human Subjects

- Ethical issues in preclinical (animal) studies:Basic philosophies of animal ethics: (3 „R"s), Animal Ethics Committee,
- Institutional Ethics Committees for human research: constitution and practices
- Institutional Review Board, Special issues in research.
- Ethical Guidelines-ICMR,
- Ethics-SOPs Ethical issues based on methodology of clinical Research.
- The ethics of clinical research in developing countries.
- Liability and indemnity in clinical trials (Insurance and Indemnity: roles and responsibility) •
- Ethics and clinical trials in special population •Ethics in clinical research publication; publication policy, Canadian guidelines.
- Clinical Research regulations in India – CDSCO guidelines, ICMR guidelines
- Drugs and Cosmetics Act 1940 , Schedule Y
- New Drug and Clinical Trials Rules 2019
- Clinical Trial Application in India
- Import & Export of Drugs in India
- Investigational New Drug application (IND)
- Abbreviated New Drug Application (ANDA)
- New Drug Application (NDA)
- USFDA regulations to conduct drug studies
- Clinical Research regulations in UK – Medicines and Healthcare Products Regulatory Agency (MHRA) • Clinical Research regulations in Europe (EMEA)
- General concepts Intellectual Property Rights & International Institutions
- Patent Laws Introduction to Copyrights and Trademark

- **Text Books and References:**

- Central Drugs Standard Control Organization. Good Clinical Practices-Guidelines for Clinical Trials on Pharmaceutical Products in India. New Delhi: Ministry of Health; 2001.

- International Conference on Harmonization of Technical requirements for registration of Pharmaceuticals for human use. ICH Harmonized Tripartite Guideline. Guideline for Good Clinical Practice.E6; May 1996.
- Ethical Guidelines for Biomedical Research on Human Subjects 2000. Indian Council of Medical Research, New Delhi.
- Sandy Weinberg. Guidebook For Drug Regulatory Submissions. A John Wiley & Sons, inc.,2009
- Indian GCP – Central Drugs Standard Control Organization.
- Good Clinical Practices– Guidelines for Clinical Trials on Pharmacuetical Products in India. New Delhi: Ministry of Health; 2001. Schedule Y
- FDA Regulatory affairs: Dougles J. Posano& David Mantus.
- Introduction to regulatory affairs: Vedjignesh.
- A guide book for regulatory submission: Sandy Weinberg

- **Practical:**

1. To prepare and submit Informed Consent Form (ICF) for the following population
- Geriatric Patients
- Pediatric patients
- Psychiatric patients
- Unconscious patients

2 To prepare protocol for dummy clinical data with emphasison guidelines regulations and ethics

5. Clinical Trial Documentation

- **Course Objective:**
- To enrich the student's role and responsibility in clinical trial documentation in clinical trials.
- To know the importance of clinical trial documentation in clinical research.
- **Course Contents:**
- **Clinical trial Documents**
- Guidelines to the preparation of following documents:

- Protocols, Investigator's Brochure, Informed Consent Form, Case report forms, Contracts and agreements,
- Trial Master File preparation and maintenance,
- Investigator Site File, Pharmacy File, Diary Cards

- **Clinical Trial Start up activities**
- Site Feasibility Studies,
- Site/Investigator selection,
- Pre-study visit, Investigator meeting, Clinical trial agreement execution,
- Ethics committee document preparation and submission,
- Site initiation visit
- Investigational Product: Procurement and Storage of investigation product

- **Preparation and conduct of monitoring visit**
- Review of source documents, CRF, ICF, IP storage, accountability and reconciliation,
- Study Procedure, EC communications, Safety reporting,
- Monitoring visit reporting and follow-up Close-Out visit:
- Study related documents collection,
- Archival requirement,
- Investigational Product reconciliation and destruction,
- Close-Out visit report.

- **Quality Assurance and Quality Control in Clinical Trials**
- Audit criteria, Audit process,
- Responsibilities of stakeholders in audit process,
- Audit follow-up and documentation,
- Audit resolution and Preparing for FDA inspections,
- Fraud and misconduct management
- **Fundamentals of Medical Writing & Data interpretation and presentation:**
- **The Clinical Study Report & Reporting clinical laboratory tests**
- **Preparation of Investigator's Brochure, clinical summaries and global submission dossiers**

- **Bibliography preparation ,Computer skills & Language for medical writers :**
- **RECOMMENDED BOOKS: Theory**
- 1.Handbook of clinical research. Julia Lloyd and Ann Raven Ed. Churchill Livingstone c.
- 2. Principles of Clinical Research edited by Giovanna di Ignazio, Di Giovanna and Haynes
- **Reference books:**
- 1. Recent Central Drugs Standard Control Organization. Good Clinical Practices-Guidelines for Clinical Trials on Pharmaceutical Products in India. New Delhi: Ministry of Health;2013, 2017.
- 2. International Conference on Harmonization of Technical requirements for registration of Pharmaceuticals for human use. ICH Harmonized Tripartite Guideline. Guideline for Good Clinical Practice.E6; May 1996.
- 3. Ethical Guidelines for Biomedical Research on Human Subjects 2000, 2014, 2017. Indian Council of Medical Research, New Delhi.
- 4. Textbook of Clinical Trials edited by David Machin, Simon Day and Sylvan Green,March 2005, John Wiley and Sons. 5. Clinical Data Management edited by R K Rondels, S A Varley, C F Webbs. SecondEdition, Jan 2000, Wiley Publications

- **Practical:**
- 1. To prepare and submit Informed Consent Process (ICF) for the following population
- Geriatric Patients
- Pediatric patients
- Psychiatric patients
- Unconscious patients
- To prepare and submit dummy patient information sheet (PIS) for the below mentioned population
- Geriatric Patients
- Pediatric patients
- Psychiatric patients
- Unconscious patients
- To prepare and submit the standard operating procedures(SOP) for procurement and storage filing of Investigational product(IP)
- To prepare and submit e-CRF(Electronic Case Report Form) for dummy clinical data

- To prepare protocol , Investigator's Brochure, clinical summaries and global submission dossiers for dummy clinical data

6. Clinical Data Management and Biostatistics

- **Course Objective:**
- To enrich the understanding of clinical data management procedure in clinical research which sponsor, CRO and Hospital use for clinical trials.
- To know the latest technology of clinical data management used in clinical trials
- **Course Contents:**

- Infrastructure and System Requirement for Data Management:
- Electronic data capture systems,
- Selection and implementation of new systems,
- System validation and test procedures,
- Coding dictionaries,
- Data migration and archival Clinical Trial Data Management:
- Standard Operating Procedures (SOPs)
- , Data management plan,
- Case Record Form (CRF)& Data base design considerations,
- Study set-up, Data entry, CRF tracking and corrections, Central lab, IVRS, source data.
- Data cleaning, managing laboratory and ADR data, Data transfer and database lock,
- Quality Control and Quality Assurance in CDM,
- Data mining and warehousing

Text & References:

- Clinical Data Management: 2nd Edition by Richard K. Rondel, Sheila A. Varley, Colin F. Webb
- Practical Guide to Clinical Data Management by Susanne Prokscha - Taylor & Francis

• Biostatistics

- Organization and display of data,
- Types of data,
- Graphical diagrammatic representation of data.
- Measures of Central tendency, Mean, median, mode,
- Measure of dispersion: Standard Deviation, Standard Error, Variance, range, Coefficient of Variation.
- Statistical input during protocol design,
- Demonstration of sample size calculation
- Role of biostatisticians in clinical research,
- Parametric and Non Parametric statistical tests: t-test & chi-square test , ANOVA etc
- Incidence and prevalence, relative risk, attributable risk
- Basics of testing hypothesis a) Null hypothesis, level of significance, power of test, P value, statistical estimation of confidence intervals.
- b) Basics of statistical softwares: SPSS, Epi Info, SAS

• Text & References:

- Text: • Biostatistics: A foundation for analysis in the Health Sciences, W.W Daniel. Publisher: John Wiley and Sons.
- Biostatistics, P.N Arora and P.K Malhan. Publisher: Himalaya Publishing House.
- References: •Introduction to Biostatistics, Ronald N. Forthfer and Eun Sun Lee .Publisher: Elsevier.
- Biostatistics: A foundation for analysis in the Health Sciences, W.W Daniel. Publisher: John Wiley and Sons.
- Statistical Methodology, S.P Gupta.
- . • Biostatistics: A manual of Statistical Methodology for use in Health, Nutrition and Anthropology, K. Visweswara Rao.

- **PRACTICAL**

- 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.Basic introduction to SPSS and other important softwares

Examination Scheme for all subjects in I Semester and II Semester

Components	Theory Examination	Practical Examination	Viva	Assignment/ Project/Seminar/Quiz	Total (Theory + Practical)
Weightage (In Marks)	50	30	10	10	100

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