

Table - 7: Course of study for M. Pharm. (Regulatory Affairs)

Course Code	Course	Credit Hours	Credit Points	Hrs./wk	Marks
Semester I					
MRA 101T	Good Regulatory Practices	4	4	4	100
MRA 102T	Documentation and Regulatory Writing	4	4	4	100
MRA 103T	Clinical Research Regulations	4	4	4	100
MRA 104T	Regulations and Legislation for Drugs & Cosmetics, Medical Devices, Biologicals & Herbals, and Food & Nutraceuticals In India and Intellectual Property Rights	4	4	4	100
MRA 105P	Regulatory Affairs Practical I	12	6	12	150
	Seminar/Assignment	7	4	7	100
	Total	35	26	35	650
Semester II					
MRA 201T	Regulatory Aspects of Drugs & Cosmetics	4	4	4	100
MRA 202T	Regulatory Aspects of Herbal & Biologicals	4	4	4	100
MRA 203T	Regulatory Aspects of Medical Devices	4	4	4	100
MRA 204T	Regulatory Aspects of Food & Nutraceuticals	4	4	4	100
MRA 205P	Regulatory Affairs Practical II	12	6	12	150
	Seminar/Assignment	7	4	7	100
	Total	35	26	35	650

PHARMACEUTICAL REGULATORY AFFAIRS (MRA)

GOOD REGULATORY PRACTICES (MRA 101T)

Scope

This course is designed to impart fundamental knowledge on various Good Regulatory Practices viz., cGMP, GLP, GALP and GDP for Pharmaceuticals, Cosmetics, Food & Nutraceuticals, Medical devices, In-vitro Diagnostic Medical Devices (IVDs) and biological products and understand the rationale behind these requirements and will propose ways and means of complying with them.

Objectives

At completion of this course it is expected that students will be able to understand,

- The key regulatory and compliance elements with respect to Good Manufacturing Practices, Good Laboratory Practices, Good Automated Laboratory Practices and Good Documentation Practices.
- Prepare and implement the check lists and SOPs for various Good Regulatory Practices
- Implement Good Regulatory Practices in the Healthcare and related Industries
- Prepare for the readiness and conduct of audits and inspections.

THEORY

60 Hrs

1. Current Good Manufacturing Practices: Introduction, US cGMP Part 210 and Part 211. EC Principles of GMP (Directive 91/356/EEC) Article 6 to Article 14 and WHO cGMP guidelines GAMP-5; Medical device and IVDs Global Harmonization Task Force (GHTF) Guidance docs. 12 Hrs
2. Good Laboratory Practices: Introduction, USFDA GLP Regulations (Subpart A to Subpart K), Controlling the GLP inspection process, Documentation, Audit, goals of Laboratory Quality Audit, Audit tools, Future of GLP regulations, relevant ISO and Quality Council of India (QCI) Standards 12 Hrs
3. Good Automated Laboratory Practices: Introduction to GALP, Principles of GALP, GALP Requirements, SOPs of GALP, Training Documentation, 21 CFR Part 11, General check list of 21 CFR Part 11, Software Evaluation checklist, relevant ISO and QCI Standards. 12 Hrs

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| 4 | Good Distribution Practices: Introduction to GDP, Legal GDP requirements put worldwide, Principles, Personnel, Documentation, Premises and Equipment, Deliveries to Customers, Returns, Self-Inspection, Provision of information, Stability testing principles, WHO GDP, USP GDP (Supply chain integrity), relevant CDSCO guidance and ISO standards | 12
Hrs |
| 5 | Quality management systems: Concept of Quality, Total Quality Management, Quality by design, Six Sigma concept, Out of Specifications (OOS), Change control. Validation: Types of Validation, Types of Qualification, Validation master plan (VMP), Analytical Method Validation. Validation of utilities, [Compressed air, steam, water systems, Heat Ventilation and Air conditioning (HVAC)]and Cleaning Validation. The International Conference on Harmonization (ICH) process, ICH guidelines to establish quality, safety and efficacy of drug substances and products, ISO 13485, Sch VIII and other relevant CDSCO regulatory guidance documents. | 12
Hrs |

REFERENCES

1. Good Laboratory Practice Regulations, by Sandy Weinberg, Fourth Edition Drugs and the Pharmaceutical Sciences, Vol.168
2. Good Pharmaceutical Manufacturing practice, Rational and compliance by John Sharp, CRC Press
3. Establishing a cGMP Laboratory Audit System, A practical Guide by David M.Bleisner, Wiley Publication.
4. How to practice GLP by PP Sharma, Vandana Publications.
5. Laboratory Auditing for Quality and Regulatory compliance bu Donald C.Singer, Drugs and the Pharmaceutical Sciences, Vol.150.
6. Drugs & Cosmetics Act, Rules & Amendments

DOCUMENTATION AND REGULATORY WRITING (MRA 102T)

Scope

This course is designed to impart fundamental knowledge on documentation and general principles involved in regulatory writing and submission to agencies.

Objectives

Upon completion of the course the student shall be able to,

- Know the various documents pertaining to drugs in pharmaceutical industry
- Understand the basics of regulatory compilation
- Create and assemble the regulation submission as per the requirements of agencies
- Follow up the submissions and post approval document requirements

THEORY

60 Hrs

1. Documentation in pharmaceutical industry: Exploratory 12
Product Development Brief (EPDB) for Drug substance and Drug Hrs
product, Product Development Plan (PDP), Product Development
Report (PDR), Master Formula Record, Batch Manufacturing
Record and its calculations, Batch Reconciliation, Batch
Packaging Records, Print pack specifications, Distribution
records, Certificate of Analysis (CoA), Site Master File and Drug
Master Files (DMF).

- 2 Dossier preparation and submission: Introduction and 12
overview of dossiers, contents and organization of dossier, Hrs
binders and sections, compilation and review of dossier. Paper
submissions, overview and modules of CTD, electronic CTD
submissions; Electronic submission: Planning electronic
submission, requirements for submission, regulatory bindings and
requirements, Tool and Technologies, electronic dossier
submission process and validating the submission, Electronic
Submission Gateway (ESG). Non eCTD electronic submissions
(NeeS), Asian CTD formats (ACTD) submission. Organizing,
process and validation of submission. Submission in Sugam
system of CDSCO.

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| 3 | Audits: Introduction, Definition, Summary, Types of audits, GMP compliance audit, Audit policy, Internal and External Audits, Second Party Audits, External third party audits, Auditing strategies, Preparation and conducting audit, Auditing strategies, audit analysis, audit report, audit follow up. Auditing/inspection of manufacturing facilities by regulatory agencies. Timelines for audits/inspection. GHTF study group 4 guidance document. ISO 13485. | 12
Hrs |
| 4 | Inspections: Pre-approval inspections, Inspection of pharmaceutical manufacturers, Inspection of drug distribution channels, Quality systems requirements for national good manufacturing practice inspectorates, inspection report, model certificate of good manufacturing practices, Root cause analysis, Corrective and Preventive action (CAPA). | 12
Hrs |
| 5 | Product life cycle management: Prior Approval Supplement (PAS), Post Approval Changes [SUPAC], Changes Being Effected in 30 Days (CBE-30), Annual Report, Post marketing Reporting Requirements, Post approval Labeling Changes, Lifecycle Management, FDA Inspection and Enforcement, Establishment Inspection Report (EIR), Warning Letters, Recalls, Seizure and Injunctions. ISO Risk Management Standard | 12
Hrs |

REFERENCES

1. Compliance auditing for Pharmaceutical Manufacturers. Karen Ginsbury and Gil Bismuth, Interpharm/CRC, Boca Raton, London New York, Washington D.C.
2. Pharmaceutical Manufacturing Handbook, Regulations and Quality by Shayne Cox Gad. Wiley-Interscience, A John Wiley and sons, Inc., Publications.
3. Handbook of microbiological Quality control. Rosamund M. Baird, Norman A. Hodges, Stephen P. Denyar. CRC Press. 2000.
4. Laboratory auditing for quality and regulatory compliance. Donald C. Singer, Raluca-loana Stefan, Jacobus F. Van Staden. Taylor and Francis (2005).
5. Implementing Juran's Road Map for Quality Leadership: Benchmarks and Results, By Al Endres, Wiley, 2000
6. Understanding, Managing and Implementing Quality: Frameworks, Techniques and Cases, By Jiju Antony; David Preece, Routledge, 2002

7. Organizing for High Performance: Employee Involvement, TQM, Reengineering, and Knowledge Management in the Fortune 1000: The CEO Report By Edward E. Lawler; Susan Albers Mohrman; George Benson, Jossey-Bass, 2001
8. Corporate Culture and the Quality Organization By James W. Fairfield-Sonn, Quorum Books, 2001
9. The Quality Management Sourcebook: An International Guide to Materials and Resources By Christine Avery; Diane Zabel, Routledge, 1997
10. The Quality Toolbox, Second Edition, Nancy R. Tague, ASQ Publications
11. Juran's Quality Handbook, Sixth Edition, Joseph M. Juran and Joseph A. De Feo, ASQ Publications
12. Root Cause Analysis, The Core of Problem Solving and Corrective Action, Duke Okes, 2009, ASQ Publications
13. International Medical Device Regulators Forum (IMDRF) Medical Device Single Audit Program (MDSAP)

Library
G.Pulla Reddy College of Pharmacy
Hyderabad

**SUBJECT : CLINICAL RESEARCH REGULATIONS
(MRA 103T)**

UNIT I Clinical Drug Development Process

Different types of Clinical Studies

Phases of clinical trials, Clinical Trial protocol

Phase 0 studies

Phase I and subtype studies (single ascending, multiple ascending, dose escalation, methods, food effect studies, drug – drug interaction, PK end points

Phase II studies (proof of concept or principle studies to establish efficacy)

Phase III studies (Multi ethnicity, global clinical trial, registration studies)

Phase IV studies (Post Marketing Studies; PSUR)

Clinical Investigation and Evaluation of Medical Devices & IVDs

Key Concepts of Medical Device Clinical Evaluation

Key concepts of Clinical Investigation

UNIT II Ethics in Clinical Research:

Historical Perspectives: Nuremberg Code, Thalidomide study, Nazis Trials, Tuskegee Syphilis Study, The Belmont Report, The declaration of Helsinki

Origin of International Conference on Harmonization – Good Clinical Practice (ICH-GCP) guidelines.

The ethics of randomized clinical trials

The role of placebo in clinical trials

Ethics of clinical research in special population

Institutional Review Board/Independent Ethics Committee/Ethics

Committee – composition, roles, responsibilities, review and approval process and ongoing monitoring of safety data

Data safety monitoring boards.

Responsibilities of sponsor, CRO, and investigator in ethical conduct of clinical research

Ethical principles governing informed consent process

Patient Information Sheet and Informed Consent Form

The informed consent process and documentation

UNIT III Regulations governing Clinical Trials

India: Clinical Research regulations in India – Schedule Y & Medical Device Guidance---

NDCT 2019 (clinical trial, bioavailability and bioequivalence study of new drugs and investigational new drugs, general principles and practices for clinical trial, conduct of clinical trial, post market assessment and medical device rules 2017

USA: Regulations to conduct drug studies in USA (FDA)

NDA 505(b)(1) of the FD&C Act (Application for approval of a new drug)

NDA 505(b)(2) of the FD&C Act (Application for approval of a new drug that relies, at least in part, on data not developed by the applicant)

ANDA 505(j) of the FD&C Act (Application for approval of a generic drug product)

FDA Guidance for Industry - Acceptance of Foreign Clinical Studies

FDA Clinical Trials Guidance Document: Good Clinical Practice

EU: Clinical Research regulations in European Union (EMA)

UNIT IV Clinical Research Related Guidelines

Indian GCP Guidelines

ICMR Ethical Guidelines for Biomedical Research

CDSCO guidelines

GHTF study group 5 guidance documents

Regulatory Guidance on Efficacy and Safety ICH Guidance's

E4 – Dose Response Information to support Drug Registration

E7 – Studies in support of General Population: Geriatrics

E8 – General Considerations of Clinical Trials

E10 – Choice of Control Groups and Related Issues in Clinical Trials,

E 11 – Clinical Investigation of Medicinal Products in the Pediatric Population

General biostatistics principle applied in clinical research

UNIT V USA & EU Guidance

USA: FDA Guidance

CFR 21Part 50: Protection of Human Subjects

CFR 21Part 54: Financial Disclosure by Clinical Investigators

CFR 21Part 312: IND Application

CFR 21Part 314: Application for FDA Approval to Market a New Drug

CFR 21Part 320: Bioavailability and bioequivalence requirements
CFR 21Part 812: Investigational Device Exemptions
CFR 21Part 822: Post-market surveillance
FDA Safety Reporting Requirements for INDs and BA/BE Studies
FDA Med Watch
Guidance for Industry: Good Pharmacovigilance Practices and
Pharmacoepidemiologic Assessment
European Union: EMA Guidance
EU Directives 2001
EudraLex (EMA) Volume 3 – Scientific guidelines for medicinal
products for human use
EU Annual Safety Report (ASR)
Volume 9A – Pharmacovigilance for Medicinal Products for Human
Use
EU MDR with respect to clinical research
ISO 14155

REFERENCES

1. Clinical Trials and Human Research: A Practical Guide to Regulatory Compliance By Fay A. Rozovsky and Rodney K. Adams
2. HIPAA and Human Subjects Research: A Question and Answer Reference Guide By Mark Barnes, JD, LLM and Jennifer Kulynych, JD, PhD
3. Principles and Practices of Clinical Research, Second Edition Edited by John I. Gallin and Frederick P. Ognibene
4. Reviewing Clinical Trials: A Guide for the Ethics Committee; Johan PE Karlberg and Marjorie A Speers; Karlberg, Johan Petter Einar, Hong Kong.
5. International Pharmaceutical Product Registration: Aspects of Quality, Safety and Efficacy; Anthony C. Cartwright; Taylor & Francis Inc., USA.
6. New Drug Approval Process: The Global Challenge; Guarino, Richard A; Marcel Dekker Inc., NY.
7. FDA regulatory affairs: a guide for prescription drugs, medical devices, and biologics; Douglas J. Pisano, David Mantus; CRC Press, USA
8. Country Specific Guidelines from official websites.
9. Drugs & Cosmetics Act & Rules and Amendments

RECOMMENDED WEBSITES:

1. EU Clinical Research Directive 2001: <http://www.eortc.be/services/doc/clinical-eudirective-04-april-01.pdf>
2. Code of Federal Regulations, FDA: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/cfrsearch.cfm>
3. Guidelines of International Conference on Harmonization: <http://www.ich.org/products/guidelines.html>
4. Eudralex Guidelines: <http://www.gmpcompliance.info/euguide.htm>
5. FDA New Drug Application:
6. <http://www.fda.gov/regulatoryinformation/legislation/FederalFoodDrugandCosmeticActFDCAct/FDCActChapterVDrugsandDevices/ucm108125.htm>
7. Medicines and Healthcare products Regulatory Agency: <http://www.mhra.gov.uk>
8. Central Drugs Standard Control Organization Guidance for Industry: <http://cdsco.nic.in/CDSCO-GuidanceForIndustry.pdf>
9. ICMR Ethical Guidelines for Biomedical Research: http://icmr.nic.in/ethical_guidelines.pdf

**REGULATIONS AND LEGISLATION FOR DRUGS & COSMETICS,
MEDICAL DEVICES, BIOLOGICALS & HERBALS, AND FOOD &
NUTRACEUTICALS IN INDIA AND INTELLECTUAL PROPERTY
RIGHTS
(MRA 104T)**

Scope

This course is designed to impart fundamental knowledge on regulations and legislation in India w.r.t. Drugs & Cosmetics, Medical Devices, Biologicals & Herbals, and Food & Nutraceuticals. It prepares the students for basic regulatory requirements in India of Drugs & Cosmetics, Medical Devices, Biologicals & Herbals, and Food & Nutraceuticals. for manufacture, import & registration, export, sale, marketing authorization, clinical trials and intellectual property rights.

Objectives

Upon the completion of the course the student shall be able to:

- Know different Acts and guidelines that regulate Drugs & Cosmetics, Medical Devices, Biologicals & Herbals, and Food & Nutraceuticals industry in India.
- Understand the approval process and regulatory requirements for Drugs & Cosmetics, Medical Devices, Biologicals & Herbals, and Food & Nutraceuticals

THEORY

60 Hrs

1. Biologicals & Herbals, and Food & Nutraceuticals Acts and Rules (with latest amendments):

12
Hrs

1. Drugs and Cosmetics Act 1940 and Rules 1945: DPCO and NPPA
2. Other relevant provisions (rules schedules and guidelines for approval of Drugs & Cosmetics, Medical Devices, Biologicals & Herbals, and Food & Nutraceuticals in India

Other relevant Acts: Narcotics Drugs and Psychotropic Substances Act; Medicinal and Toilet Preparations (Excise Duties) Act, 1955; Pharmacy Act, 1948; Drugs and Magic Remedies (Objectionable Advertisements) Act, 1955; Prevention of Cruelty to Animals Act.

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| 2 | Regulatory requirements and approval procedures for Drugs & Cosmetics Medical Devices, Biologicals & Herbals, and Food & Nutraceuticals
CDSCO (Central Drug Standard Control Organization) and State Licensing Authority: Organization, Responsibilities <ul style="list-style-type: none"> • Rules, regulations, guidelines and standards for regulatory filing of Drugs & Cosmetics, Medical Devices, Biologicals & Herbals, and Food & Nutraceuticals • Format and contents of Regulatory dossier filing Clinical trial/ investigations | 12
Hrs |
| 3 | Indian Pharmacopoeial Standards, BIS standards and ISO and other relevant standards | 12
Hrs |
| 4 | Bioavailability and Bioequivalence data (BA &BE), BCS Classification of Drugs, Regulatory Requirements for Bioequivalence study
Stability requirements: ICH and WHO

Guidelines for Drug testing in animals/Preclinical Studies

Animal testing: Rationale for conducting studies, CPCSEA Guidelines
Ethical guidelines for human participants
ICMR-DBT Guidelines for Stem Cell Research | 12
Hrs |
| 5 | Intellectual Property Rights: Patent, Trademark, Copyright, Industrial Designs and Geographical Indications, Indian Patent Scenario. IPR vs Regulatory Affairs | 12
Hrs |

REFERENCES

1. Manual of Patent Practice & Procedure, 3rd Edition, by The Patent Office of India
2. Patent Failure How Judges, Bureaucrats, and Lawyers put innovators at risk by James Bessen and Michael J. Meurer
3. Principles and Practice of Clinical Trial Medicine by Richard Chin and Bruce Y. Lee
4. Ethical Guidelines for Biomedical Research on Human Participants by Indian Council of Medical Research New delhi 2006.
5. CPCSEA Guidelines for Laboratory Animal Facility by Committee for the purpose of control and supervision on experiments on animals (CPCSEA)

6. ICH E6 Guideline — Good Clinical Practice|| by ICH Harmonised Tripartite
7. Guidance for Industry on Submission of Clinical Trial Application for Evaluating Safety and Efficacy by CDSCO (Central Drug Standard Control Organisation)
8. Guidance for Industry on Requirement of Chemical & Pharmaceutical Information including Stability Study Data before approval of clinical trials / BE studies by CDSCO
9. Guidelines for Import and Manufacture of Medical Devices by CDSCO
10. Guidelines from official website of CDSCO

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REGULATORY AFFAIRS PRACTICAL I

(MRA 105P)

1. Case studies (4 Nos.) of each of Good Pharmaceutical Practices.
2. *a) Preparation and evaluation of tablets*
b) Documentation for in process and finished products Quality control tests for Solid (to be removed), liquid, Semisolid and Sterile preparations.
3. Preparation of SOPs, Analytical reports (Stability and validation)
4. Protocol preparation for documentation of various types of records (BMR, MFR, DR)
5. Labeling comparison between brand & generics.
6. Preparation of clinical trial protocol for registering trial in India
7. Registration for conducting BA/ BE studies in India
8. Import of drugs for research and developmental activities
9. Preparation of regulatory dossier as per Indian CTD format and submission in SUGAM
10. Registering for different Intellectual Property Rights in India
11. GMP Audit Requirements as per CDSCO
12. Preparation and documentation for Indian Patent application.
13. Preparation of checklist for registration of IND as per ICH CTD format.
14. Preparation of checklist for registration of NDA as per ICH CTD format.
15. Preparation of checklist for registration of ANDA as per ICH CTD format.
16. Case studies on response with scientific rationale to USFDA Warning Letter
17. Preparation of submission checklist of IMPD for EU submission.
18. Comparison study of marketing authorization procedures in EU.
19. Comparative study of DMF system in US, EU and Japan
20. Preparation of regulatory submission using eCTD software
21. Preparation of Clinical Trial Application (CTA) for US submission
22. Preparation of Clinical Trial Application (CTA) for EU submission

23. Comparison of Clinical Trial Application requirements of US, EU and Japan of a dosage form.
24. Regulatory requirements checklist for conducting clinical trials in India.
25. Regulatory requirements checklist for conducting clinical trials in Europe.
26. Regulatory requirements checklist for conducting clinical trials in USA