Nirma University

Institute of Pharmacy

Teaching & Examination Scheme of (M. Pharm. - Regulatory Affairs)

Semester I

Sr. No.	Course Code	Course Title	Teaching Scheme				Examination Scheme				
			L	LPW/PW	T	C	Duration		Component Weightage		
							SEE	LPW/ PW	CE	LPW/ PW	SEE
1	MRA101T	Good Regulatory Practices	4	-	-	4	3.0	-	0.60	-	0.40
2	MRA102T	Documentation and Regulatory Writing	4	-	-	4	3.0	-	0.60	-	0.40
3	MRA103T	Clinical Research Regulations	4	-	-	4	3.0	-	0.60	-	0.40
4	MRA104T	Regulations and Legislation for Drugs & Cosmetics, Medical Devices, Biologicals & Herbals, and Food & Nutraceuticals In India and Intellectual Property Rights	4	-	-	4	3.0	-	0.60	-	0.40
5	MRA105P	Regulatory Affairs Practical I	-	12	-	6	-	6.0	-	1.00	-
6	MRA106S	Seminar/Assignment-I	-	7	-	4	-	-	-	1.00	-
		Total	**16**	**19**	**-**	**26**	-	-	-	-	-
			35								

L: Lectures, P/T: Practicals/Tutorial, C: Credits
LPW/PW: Laboratory / Project Work
SEE: Semester End Examination
CE: Continuous Evaluation

NIRMA UNIVERSITY

Institute of Pharmacy

(M.Pharm. - Regulatory Affairs)

(Semester – I)

L	T	P	C
4	-	-	4

Course Code	**MRA101T**
Course Title	**Good Regulatory Practices**

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,

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

Course Learning Outcomes (CLO):

At the end of the course, students will be able to –

1. Understand the concepts of cGMP and GLP
2. Describe the guidance documents for medical device and IVDs
3. Discuss principles and requirements of GALP
4. Review supply chain integrity in GDP
5. Utilize the various elements of QMS
6. Prepare SOP for equipments and processes

Syllabus: **Teaching hours**: **60 Hours**

UNIT – I **12 Hours**

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.

UNIT – 2 **12 Hours**

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

UNIT – III **12 Hours**

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 21CFR Part 11, Software Evaluation checklist, relevant ISO and QCI Standards.

UNIT – IV **12 Hours**

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

UNIT – V **12 Hours**

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 MIII and other relevant CDSCO regulatory guidance documents.

Suggested Readings^: (Latest edition)

1. Weinberg, S. Good Laboratory Practice Regulations. Informa Healthcare.
2. Robinson, D. Good Pharmaceutical Manufacturing Practice: Rationale and Compliance by John Sharp. CRC Press.
3. Bliesner, D. M. Establishing a CGMP Laboratory Audit System: A Practical Guide. John Wiley & Sons.
4. Sharma, P. P. How to Practice GLP Good Laboratory Practice. Vandana Publications.
5. Singer, D. C., Stefan, R. I., & Van Staden, J. F. Laboratory Auditing for Quality and Regulatory Compliance. Taylor & Francis.
6. Drugs & Cosmetics Act, Rules & Amendments.

L= Lecture, T= Tutorial, P= Practical, C= Credit

^ this is not an exhaustive list

(M.Pharm. - Regulatory Affairs)

(Semester – I)

L	T	P	C
4	-	-	4

Course Code	MRA102T
Course Title	Documentation and Regulatory Writing

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,

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

Course Learning Outcomes (CLO):

At the end of the course, students will be able to –

1. List the different types of documents required for drug product management
2. Understand the concept, content and format of CTD and eCTD submission
3. Describe various types of audits and audit strategies for manufacturing facilities
4. Explain the inspection process of pharmaceutical manufacturing practices along with CAPA
5. Express life cycle management of different types of pharmaceutical dosage form

Syllabus: **Teaching hours**: **60 Hours**

UNIT – I **12 Hours**

Documentation in pharmaceutical industry: Exploratory Product Development Brief (EPDB) for Drug substance and Drug 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).

UNIT – II **12 Hours**

Dossier preparation and submission: Introduction and overview of dossiers, contents and organization of dossier, 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.

UNIT – III **12 Hours**

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.

UNIT – IV **12 Hours**

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).

UNIT – V **12 Hours**

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

Suggested Readings^: (Latest edition)

1. Ginsbury, K., & Bismuth, G. Compliance Auditing for Pharmaceutical Manufacturers: A Practical Guide to In-Depth Systems Auditing. CRC Press.
2. Gad, S. C. (Ed.). Pharmaceutical manufacturing handbook: regulations and quality (Vol. 6). John Wiley & Sons.
3. Baird, R. M., Hodges, N. A., & Denyer, S. P. (Eds.). Handbook of Microbiological Quality Control in Pharmaceuticals and Medical Devices. CRC Press.
4. Singer, D. C., Stefan, R. I., & Van Staden, J. F. Laboratory Auditing for Quality and Regulatory Compliance. Taylor & Francis.
5. Endres, A. Implementing Juran's Road Map for Quality Leadership: Benchmarks and Results. John Wiley & Sons.
6. Antony, J., & Preece, D. (Eds.). Understanding, Managing and Implementing Quality: Frameworks, Techniques and Cases. Routledge.
7. Lawler, E. E., Mohrman, S. A., & Benson, G. Organizing For High Performance: Employee Involvement, TQM, Reengineering, and Knowledge Management in the Fortune 1000: The CEO report. Jossey-Bass.
8. Fairfield-Sonn, J. W. Corporate Culture and the Quality Organization. Greenwood Publishing Group.
9. Avery, C., & Zabel, D. The Quality Management Sourcebook: An International Guide to Materials and Resources. Routledge.
10. Tague,N. The Quality Toolbox. ASQ Publications
11. Joseph, M., Feo, J. Juran's Quality Handbook. ASQ Publications.
12. Okes, D. Root Cause Analysis: The Core of Problem Solving and Corrective Action-Chapter 1.ASQ Publications.
13. International Medical Device Regulators Forum (IMDRF) Medical Device Single Audit Program (MDSAP).

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(M.Pharm. - Regulatory Affairs)

(Semester – I)

L	T	P	C
4	-	-	4

Course Code	**MRA103T**
Course Title	**Clinical Research Regulations**

Scope

This course is designed to impart the fundamental knowledge on the clinical development process of drugs, pharmaceuticals and Medical Devices, phases and conduct of clinical trials and research, regulations and guidance governing the conduct of clinical research in India, USA and EU. It prepares the students to learn in detail on various laws, legislations and guidance related to safety, efficacy, ethical conduct and regulatory approval of clinical research.

Objectives

Upon completion of the course, the student shall be able to (know, do and appreciate)

1. History, origin and ethics of clinical and biomedical research and evaluation
2. Clinical drug, medical device development process and different types and phases of clinical trials
3. Regulatory requirements and guidance for conduct of clinical trials and research

Course Learning Outcomes (CLO):

At the end of the course, students will be able to –

1. Understand different phases of clinical trials for drug development process
2. Describe the importance of ethics and documentation for clinical trials
3. Differentiate clinical research regulations for drug products filing in India, USA and Europe
4. Discuss different aspects of good clinical practices as per regulatory guidelines.
5. Prepare different modules for dossier filing in USA and Europe

Syllabus: **Teaching hours**: **60 Hours**

UNIT – I **12 Hours**

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

Different Types of Studies

Key Concepts of Medical Device Clinical Evaluation

Key concepts of Clinical Investigation

UNIT – II **12 Hours**

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 **12 Hours**

Regulations governing Clinical Trials

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

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 S **12 Hours**

Clinical Research Related Guidelines

- Good Clinical Practice Guidelines (ICH GCP E6)
- 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 biostatics principle applied in clinical research

UNIT – V ENT 12 Hours

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 (EMEA) 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 MDD with respect to clinical research
- ISO 14155

Suggested Readings^: (Latest edition)

1. Rozovsky, F. A., & Adams, R. K. Clinical Trials and Human Research: A Practical Guide to Regulatory Compliance.
2. Barnes, M., Kulynych, J. HIPAA and Human Subjects Research: A Question and Answer.
3. Gallin, J. I., & Ognibene, F. P. (Eds.). Principles and Practice of Clinical Research. Academic Press.
4. Karlberg, J. P. E., & Speers, M. A. (Eds.). Reviewing Clinical Trials: A Guide for the Ethics Committee. Clinical Trials Centre.
5. Cartwright, A. C., & Matthews, B. R. (Eds.). International Pharmaceutical Product Registration. CRC Press.
6. Guarino, R. New Drug Approval Process. Marcel Dekker Inc.
7. Pisano, D. J., & Mantus, D. FDA Regulatory Affairs. CRC Press.
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/cfcfr/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: http://www.fda.gov/regulatoryinformation/legislation/FederalFoodDrugandCosmeticActFDCAct/FDCActChapterVDrugsandDevices/ucm108125.htm
6. http://www.fda.gov/regulatoryinformation/legislation/FederalFoodDrugandCosmetic ActFDCAct/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

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(M.Pharm. - Regulatory Affairs)

(Semester – I)

L	T	P	C
4	-	-	4

Course Code	**MRA104T**
Course Title	**Regulations and Legislation for Drugs & Cosmetics, Medical Devices, Biologicals & Herbals, and Food & Nutraceuticals in India and Intellectual Property Rights**

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:

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

Course Learning Outcomes (CLO):

At the end of the course, students will be able to –

1. Understand the rules and regulations for biologicals, herbals, food and nutraceuticals
2. Describe the regulatory requirements and approval procedures for drugs, cosmetics, medical devices etc.
3. Discuss pharmacopoeial standards and other standards like BIS and ISO
4. Explain regulatory requirements for bioequivalence study
5. Tell IPR issues, patent filing, copyright and trademarks

Syllabus: **Teaching hours**: **60 Hours**

UNIT – I **12 Hours**

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

- Drugs and Cosmetics Act 1940 and Rules 1945: DPCO and NPPA
- 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.

UNIT – II **12 Hours**

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

- 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

UNIT – III **12 Hours**

Indian Pharmacopoeial Standards, BIS standards and ISO and other relevant standards

UNIT – IV **12 Hours**

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

UNIT – V **12 Hours**

Intellectual Property Rights: Patent, Trademark, Copyright, Industrial Designs and Geographical Indications, Indian Patent Scenario. IPR vs Regulatory Affairs

Suggested Readings^: (Latest edition)

1. Manual of Patent Practice & Procedure, 3rd Edition, by The Patent Office of India.
2. Bessen, J., & Meurer, M. J. (2008). Patent failure: How judges, bureaucrats, and lawyers put innovators at risk. Princeton University Press.
3. Chin, R., & Lee, B. Y. (2008). Principles and practice of clinical trial medicine. Elsevier.
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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(M.Pharm. - Regulatory Affairs)

(Semester – I)

L	T	P	C
-	-	12	6

Course Code	MRA105P
Course Title	Regulatory Affairs Practical I

Syllabus: **Teaching hours**: **180 Hours**

1. Case studies (4 Nos.) of each of Good Pharmaceutical Practices.
2. Documentation for in process and finished products Quality control tests for Solid, 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

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