DR. A.P.J. ABDUL KALAM TECHNICAL UNIVERSITY, UTTAR PRADESH, LUCKNOW

Syllabus

For

M.Pharm. (Pharmaceutical Quality Assurance)

(Effective from the Session: 2017-18)

Master of Pharmacy (M. Pharm.)

SCHEMES FOR INTERNAL ASSESSMENTS AND END SEMESTER EXAMINATIONS (SEM. I & II)
(W.E.F. Session 2017-18)

PHARMACEUTICAL QUALITY ASSURANCE-MQA

Course Code	Course	Internal Assessment				End Semester Exams		Total Marks	Credit Points
		Continuous Mode	Sessional Exams		Total	Marks	Duration		
			Marks	Duration					
Semester I									
MQA101T (New)	Modern Pharmaceutical Analytical Techniques	10	15	1 Hrs	25	75	3 Hrs	100	4
MQA102T (New)	Quality Management System	10	15	1 Hrs	25	75	3 Hrs	100	4
MQA103T (New)	Quality Control and Quality Assurance	10	15	1 Hrs	25	75	3 Hrs	100	4
MQA104T (New)	Product Development and Technology Transfer	10	15	1 Hrs	25	75	3 Hrs	100	4
MQA105P (New)	Pharmaceutical Quality Assurance Practical I	20	30	6 Hrs	50	100	6 Hrs	150	6
-	Seminar/Assignment	-	-	-	-	-	-	100	4
							Total	650	26
Semester II									
MQA201T (New)	Hazards and Safety Management	10	15	1 Hr	25	75	3 Hrs	100	4
MQA202T (New)	Pharmaceutical Validation	10	15	1 Hr	25	75	3 Hrs	100	4
MQA203T (New)	Audits and Regulatory Compliance	10	15	1 Hr	25	75	3 Hrs	100	4
MQA204T (New)	Pharmaceutical Manufacturing Technology	10	15	1 Hr	25	75	3 Hrs	100	4
MQA205P (New)	Pharmaceutical Quality Assurance Practical II	20	30	6 Hrs	50	100	6 Hrs	150	6
-	Seminar/ Assignment	-	-	-	-	-	-	100	4
							Total	650	26

Schemes for Internal Assessments and End Semester Examinations (Semester III & IV)

Course Code	Course	Internal Assessment				End Semester Exams		Total Marks	Credit Points
		Continuous Mode	Sessional Exams		Total	Marks	Duration		
			Marks	Duration					
Semester III									
MRM301T (New)	Research Methodology and Biostatistics	40	60	2 Hr	100	-	-	100	4
MRM302T (New)	Journal Club	-	-	-	25	-	-	25	1
MRM303P (New)	Discussion /Presentation (Proposal Presentation)	-	-	-	50	-	-	50	2
MRM304P (New)	Research Work	350	-	-	-	-	-	350	14
							Total	525	21
Semester IV									
MRM401T (New)	Journal Club	-	-	-	25	-	-	25	1
MRM402P (New)	Discussion / Presentation (Proposal Presentation)	-	-	-	75	-	-	75	3
MRM403P (New)	Research Work and Colloquium	-	-	-	-	400	1 Hr	400	16
							Total	500	20

PHARMACEUTICAL QUALITY ASSURANCE (MQA)

FIRST SEMESTER

MODERN PHARMACEUTICAL ANALYTICAL TECHNIQUES (MQA 101T)

Scope

This subject deals with various advanced analytical instrumental techniques for identification, characterization and quantification of drugs. Instruments dealt are NMR, Mass spectrometer, IR, HPLC, GC etc.

Objectives

After completion of course student is able to know about chemicals and excipients

- The analysis of various drugs in single and combination dosage forms
- Theoretical and practical skills of the instruments

THEORY **60 Hrs**

1. **a. UV-Visible Spectroscopy**: Introduction, theory, laws, instrumentation associated with UV-Visible spectroscopy, choice of solvents and solvent effect. Applications of UV-Visible spectroscopy, Difference/ derivative spectroscopy. **10 Hrs**

   b. IR Spectroscopy: Theory, modes of molecular vibrations, sample handling, Instrumentation of dispersive and Fourier -Transform IR spectrometer, factors affecting vibrational frequencies. Applications of IR spectroscopy and data interpretation.

   c. Spectroflourimetry: Theory of fluorescence, factors affecting fluorescence (characteristics of drugs that can be analyzed by flourimetry), quenchers, Instrumentation and applications of fluorescence spectrophotometer.

   D. Flame Emission Spectroscopy and Atomic Absorption Spectroscopy: Principle, instrumentation, interferences and applications.

2. **NMR Spectroscopy:** Quantum numbers and their role in NMR, principle, Instrumentation, solvent requirement in NMR, relaxation process, NMR signals in various compounds. Chemical shift, factors influencing chemical shift, spin-spin coupling, coupling constant, nuclear magnetic double resonance, brief outline of principles of FT-NMR and 13C NMR. Applications of NMR spectroscopy. **10 Hrs**
3. **Mass Spectroscopy:** Principle, theory, instrumentation of mass spectroscopy, different types of ionization like electron impact, chemical, field, FAB and MALDI, APCI, ESI, APPI analyzers of quadrupole and time of flight, mass fragmentation and its rules, meta stable ions, isotopic peaks. Applications of mass spectroscopy. **10 Hrs**
4. **Chromatography:** Principle, apparatus, instrumentation, chromatographic parameters, factors affecting resolution, isolation of drug from excipients, data interpretation and applications of the following: **10 Hrs**
   - Thin layer chromatography
   - High performance thin layer chromatography
   - Ion exchange chromatography
   - Column chromatography
   - Gas chromatography

- High performance liquid chromatography
- Ultra high performance liquid chromatography
- Affinity chromatography
- Gel chromatography

5. **a. Electrophoresis:** Principle, instrumentation, working conditions, factors affecting separation and applications of the following: **10 Hrs**

   a) Paper electrophoresis.
   b) Gel electrophoresis.
   c) Capillary electrophoresis.
   d) Zone electrophoresis.
   e) Moving boundary electrophoresis.
   f) Isoelectric focusing.

   b. X-ray Crystallography: Production of X-rays, different X-ray methods, Bragg's law, rotating crystal technique, X-ray powder technique, types of crystals and applications of X-ray diffraction.

6. **a. Potentiometry:** Principle, working, Ion selective electrodes and application of potentiometry. **10 Hrs**

   b. Thermal Techniques: Principle, thermal transitions and Instrumentation (Heat flux and power-compensation and designs), modulated DSC, hyper DSC, experimental parameters (sample preparation, experimental conditions, calibration, heating and cooling rates, resolution, source of errors) and their influence, advantage and disadvantages, pharmaceutical applications.

   Differential Thermal Analysis (DTA): Principle, instrumentation and advantage and disadvantages, pharmaceutical applications, derivative differential thermal analysis (DDTA).

   TGA: Principle, instrumentation, factors affecting results, advantage and disadvantages, pharmaceutical applications.

   c. Immunological Assays: RIA (Radio immune assay), ELISA, bioluminescence assays.

REFERENCES

1. Spectrometric Identification of Organic compounds by Robert M Silverstein, Sixth edition, John Wiley & Sons, 2004.
2. Principles of Instrumental Analysis by Douglas A Skoog, F. James Holler, Timothy A. Nieman, 5th edition, Eastern press, Bangalore, 1998.
3. Instrumental Methods of Analysis by Willards, 7th edition, CBS Publishers.
4. Practical Pharmaceutical Chemistry by Beckett and Stenlake, Vol II, 4th edition, CBS Publishers, New Delhi, 1997.
5. Organic Spectroscopy by William Kemp, 3rd edition, ELBS, 1991.
6. Quantitative Analysis of Drugs in Pharmaceutical Formulation by P D Sethi, 3rd Edition, CBS Publishers, New Delhi, 1997.
7. Pharmaceutical Analysis - Modern Methods – Part B by J W Munson, Vol 11, Marcel. Dekker Series
8. Spectroscopy of Organic Compounds, 2nd edn., P.S. Kalsi, Wiley Eastern Ltd., Delhi.
9. Textbook of Pharmaceutical Analysis by KA. Connors, 3rd Edition, John Wiley & Sons, 1982.
10. Introduction to Spectroscopy by Pavia D.L., Lampman G.M. and Kriz G.S., Harcourt College Publishers, Philadelphia.

11. Analytical Profile of Drug Substance (All volume) by Florey K., Academic Press, Elsevier, Massachusetts.
12. Thin Layer Chromatography: A Laboratory Handbook, Stahl E., Springer, Berlin.
13. Undergraduate Instrumental Analysis, Obonson J.W.R., Marcel Dekker Inc, New York.
14. Absorption Spectroscopy of Organic Molecules by Parikh V.H., Addison-Wesley Publishing Co., London.

QUALITY MANAGEMENT SYSTEMS
(MQA 102T)

Scope

This course is designed to impart fundamental knowledge and concepts about various quality management principles and systems utilized in the manufacturing industry. It also aids in understanding the quality evaluation in the pharmaceutical industries.

Objectives

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

- The importance of quality.
- ISO management systems.
- Tools for quality improvement.
- Analysis of issues in quality.
- Quality evaluation of pharmaceuticals.
- Stability testing of drug and drug substances.
- Statistical approaches for quality.

THEORY **60 Hrs**

1. **Introduction to Quality:** Evolution of quality, definition of quality, dimensions of quality. **12 Hrs**
   Quality as a Strategic Decision: Meaning of strategy and strategic quality management, mission and vision statements, quality policy, quality objectives, strategic planning and implementation, McKinsey 7s model, competitive analysis, management commitment to quality.
   Customer Focus: Meaning of customer and customer focus, classification of customers, customer focus, customer perception of quality, factors affecting customer perception, customer requirements, meeting customer needs and expectations, customer satisfaction and customer delight, handling customer complaints, understanding customer behavior, concept of internal and external customers. Case studies. Cost of quality: Categories of cost of quality, models of cost of quality, optimizing costs, preventing cost of quality.
2. **Pharmaceutical Quality Management:** Basics of quality management, total quality management (TQM), principles of six sigma, ISO 9001:2008, 9001:2015, ISO 14001:2004. Pharmaceutical quality management– ICH Q10, knowledge management, quality metrics, operational excellence and quality management review. OSHAS Guidelines, NABL certification and accreditation, CFR-21 part 11, WHO-GMP requirements. **12 Hrs**
3. **Six System Inspection Model:** Quality management system, production system, facility and equipment system, laboratory control system, materials system, packaging and labeling system. Concept of self inspection. **12 Hrs**
   Quality systems: Change Management/ change control.
   Deviations, Out of specifications (OOS), out of trend (OOT), Complaints: Evaluation and handling, investigation and determination of root cause, corrective & preventive actions (CAPA), returns and recalls, vendor qualification, annual product reviews, batch review and batch release. concept of IPQC, area clearance/ line clearance
4. **Drug Stability:** ICH guidelines for stability testing of drug substances and drug products. **12 Hrs**
   Study of ICH Q8, quality by design and process development report.

Quality risk management: Introduction, risk assessment, risk control, risk review, risk management tools, HACCP, risk ranking and filtering according to ICH Q9 guidelines.

5. **Statistical Process Control (SPC):** Definition and importance of SPC, quality measurement in manufacturing, statistical control charts: Concepts and general aspects, advantages of statistical control, process capability, estimating inherent or potential capability from a control chart analysis, measuring process control and quality improvement, pursuit of decreased process variability. **12 Hrs**
6. **Regulatory Compliance through Quality Management and development of Quality Culture Benchmarking:** Definition of benchmarking, reasons for benchmarking, types of benchmarking, benchmarking process, advantages of benchmarking, limitations of benchmarking. **12 Hrs**

REFERENCES

1. Implementing Juran's Road Map for Quality Leadership: Benchmarks and Results, By Al Endres, Wiley, 2000.
2. Understanding, Managing and Implementing Quality: Frameworks, Techniques and Cases, By Jiju Antony; David Preece, Routledge, 2002.
3. 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.
4. Corporate Culture and the Quality Organization By James W. Fairfield-Sonn, Quorum Books, 2001
5. The Quality Management Sourcebook: An International Guide to Materials and Resources By Christine Avery; Diane Zabel, Routledge, 1997.
6. The Quality Toolbox, Second Edition, Nancy R. Tague, ASQ Publications.
7. Juran's Quality Handbook, Sixth Edition, Joseph M. Juran and Joseph A. De Feo, ASQ Publications.
8. Root Cause Analysis, The Core of Problem Solving and Corrective Action, Duke Okes, 2009, ASQ Publications.

QUALITY CONTROL AND QUALITY ASSURANCE
(MQA 103T)

Scope

This course deals with the various aspects of quality control and quality assurance aspects of pharmaceutical industries. It covers the important aspects like cGMP, QC tests, documentation, quality certifications, GLP and regulatory affairs.

Objectives

Upon completion of this course the student should be able to

- Understand the cGMP aspects in a pharmaceutical industry.
- To appreciate the importance of documentation.
- To understand the scope of quality certifications applicable to. Pharmaceutical industries.
- To understand the responsibilities of QA & QC departments.

THEORY **60 Hrs**

1.	**Introduction:** Concept and evolution and scopes of quality control and quality assurance, good laboratory practice, GMP, overview of ICH Guidelines - QSEM, with special emphasis on Q-series guidelines. **Good Laboratory Practices:** Scope of GLP, definitions, quality assurance unit, protocol for conduct of non clinical testing, control on animal house, report preparation and documentation. CPCSEA guidelines.	**12 Hrs**
2.	cGMP Guidelines according to schedule M, USFDA (inclusive of CDER and CBER), pharmaceutical inspection convention(PIC),WHO and EMEA covering: Organization and personnel responsibilities, training, hygiene and personal records, drug industry location, design, construction and plant lay out, maintenance, sanitation, environmental control, utilities and maintenance of sterile areas, control of contamination and Good warehousing practice.	**12 Hrs**
3.	Analysis of raw materials, finished products, packaging materials, in process quality control (IPQC), developing specification (ICHQ6 and Q3), purchase specifications and maintenance of stores for raw materials. In process quality control and finished products quality control for following dosage forms in pharma industry according to Indian, US and British pharmacopoeias: tablets, capsules, ointments, suppositories, creams, parenterals, ophthalmic and surgical products (How to refer pharmacopoeias).	**12 Hrs**
4.	**Documentation in Pharmaceutical Industry:** Three tier documentation, policy, procedures and work instructions, and records (Formats). Basic principles- How to maintain, retention and retrieval etc. Standard operating procedures (How to write), master batch record, batch manufacturing record, quality audit plan and reports. Specification and test procedures, protocols and reports, distribution records, electronic data handling, concepts of controlled and uncontrolled documents. Submission documents for regulators DMFs as common technical document and electronic common technical documentation (CTD, eCTD). Concept of regulated and non regulated markets	**12 Hrs**
5.	**Manufacturing Operations and Controls:** Sanitation of manufacturing premises, mix-ups and cross contamination processing of intermediates and bulk products, packaging	**12 Hrs**

operations, IPQC, release of finished product, process deviations, charge-in of components, time limitations on production, drug product inspection, expiry date calculation, calculation of yields, production record review, change control, sterile products, aseptic process control, packaging, reprocessing, salvaging, handling of waste and scrap disposal. Introduction, scope and importance of intellectual property rights. Concept of trade mark, copyright and patents.

REFERENCES

1. Quality Assurance Guide by Organization of Pharmaceutical Procedures of India, 3rd revised edition, Volume I & II, Mumbai, 1996.
2. Good Laboratory Practice Regulations, 2nd Edition, Sandy Weinberg Vol. 69, Marcel Dekker Series, 1995.
3. Quality Assurance of Pharmaceuticals- A compedium of Guide lines and Related materials Vol I & II, 2nd edition, WHO Publications, 1999.
4. How to Practice GMP's – P P Sharma, Vandana Publications, Agra, 1991.
5. The International Pharmacopoeia – vol I, II, III, IV & V - General Methods of Analysis And Quality Specification for Pharmaceutical Substances, Excepients and Dosage forms, 3rd edition, WHO, Geneva, 2005.
6. Good laboratory Practice Regulations – Allen F. Hirsch, Volume 38, Marcel Dekker Series, 1989.
7. ISO 9000 and Total Quality Management
8. The drugs and cosmetics act 1940 – Deshpande, Nilesh Gandhi, 4th edition, Susmit Publishers, 2006.
9. QA Manual- D.H. Shah, 1st edition, Business Horizons, 2000.
10. Good Manufacturing Practices for Pharmaceuticals a plan for total quality control – Sidney H. Willig, Vol. 52, 3rd edition, Marcel Dekker Series.
11. Steinborn L. GMP/ISO Quality Audit Manual for Healthcare Manufacturers and Their Suppliers, Sixth Edition, (Volume 1 - With Checklists and Software Package). Taylor & Francis; 2003.
12. Sarker DK. Quality Systems and Controls for Pharmaceuticals. John Wiley & Sons; 2008.
13. Schedule M and Schedule N.

PRODUCT DEVELOPMENT AND TECHNOLOGY TRANSFER
(MQA 104T)

Scope

This deal with technology transfer covers the activities associated with Drug Substance, Drug Product and analytical tests and methods, required following candidate drug selection to completion of technology transfer from R&D to the first receiving site and technology transfer related to post-marketing changes in manufacturing places.

Objectives

Upon completion of this course the student should be able to

- To understand the new product development process.
- To understand the necessary information to transfer technology from R&D to actual manufacturing by sorting out various information obtained during R&D.
- To elucidate necessary information to transfer technology of existing.
- Products between various manufacturing places.

THEORY **60 Hrs**

1. **Principles of Drug Discovery and Development:** Introduction, clinical research process. development and informational content for investigational new drugs application (IND), new drug application (NDA), abbreviated new drug application (ANDA), supplemental new drug application (SNDA), scale up post approval changes (SUPAC) and bulk active chemical post approval changes (BACPAC), post marketing surveillance, product registration guidelines – CDSCO, USFDA. **12 Hrs**

2. **Pre-Formulation Studies:** Introduction/concept, organoleptic properties, purity, impurity profiles, particle size, shape and surface area. Solubility, methods to improve solubility of drugs: Surfactants & its importance, co-solvency. Techniques for the study of crystal properties and polymorphism. Pre-formulation protocol, stability testing during product development. **12 Hrs**

3. **Pilot Plant Scale Up:** Concept, significance, design, layout of pilot plant scale up study, operations, large scale manufacturing techniques (formula, equipment, process, stability and quality control) of solids, liquids, semisolid and parenteral dosage forms. New era of drug products: Opportunities and challenges. **12 Hrs**

4. **Pharmaceutical Packaging:** Pharmaceutical dosage form and their packaging requirements, pharmaceutical packaging materials, medical device packaging, enteral packaging, aseptic packaging systems, container closure systems, issues facing modern drug packaging, selection and evaluation of pharmaceutical packaging materials. **12 Hrs**
   Quality control test: Containers, closures and secondary packing materials.

5. **Technology Transfer:** Development of technology by R & D, technology transfer from R & D to production, optimization and production, qualitative and quantitative technology models. Documentation in technology transfer: Development report, technology transfer plan and exhibit. **12 Hrs**

REFERENCES

1. The Process of New Drug Discovery and Development. I and II Edition (2006) by Charles G. Smith, James T and O. Donnell. CRC Press, Group of Taylor and Francis.
2. Theory and Practice of Industrial Pharmacy by Leon Lac Lachman, Herbert A. Liberman. Marcel Dekker Inc. New York.
3. Good Manufacturing of Pharmaceuticals (A Plan for total quality control), Sidney H Willing, Murray M, Tuckerman. Williams Hitchings IV, 3rd Edition. Bhalani Publishing House Mumbai.
4. Tablets Vol. I, II, III by Leon Lachman, Herbert A. Liberman, Joseph B. Schwartz, 2nd Edn. (1989) Marcel Dekker Inc. New York.
5. Text book of Bio- Pharmaceutics and Clinical Pharmacokinetics by Milo Gibaldi, 3rd Edn, Lea & Febriger, Philadelphia.
6. Pharmaceutical Product Development by Vandana V. Patrevale. John I. Disouza. Maharukh T.Rustomji. CRC Press, Group of Taylor and Francis.
7. Dissolution, Bioavailability and Bio-Equivalence by Abdou H.M, Mack Publishing company, Eastern Pennsylvania.
8. Remingtons Pharmaceutical Sciences, by Alfonso & Gennaro, 19th Edn.(1995)OO2C Lippincott; Williams and Wilkins A Wolters Kluwer Company, Philadelphia.
9. The Pharmaceutical Sciences; the Pharma Path way ‘Pure and Applied Pharmacy’ by D. A Sawant, Pragati Books Pvt. Ltd.
10. Pharmaceutical Packaging Technology by D.A. Dean. E.R. Evans, I.H. Hall. 1st Edition (Reprint 2006). Taylor and Francis. London and New York.

QUALITY ASSURANCE PRACTICAL - I
(MQA 105P)

PRACTICALS

1. Analysis of Pharmacopoeial compounds in bulk and in their formulations (tablet/ capsules/ semisolids) by UV Vis spectrophotometer.
2. Simultaneous estimation of multi-drug component containing formulations by UV spectrophotometry.
3. Experiments based on HPLC.
4. Experiments based on Gas Chromatography.
5. Estimation of riboflavin/quinine sulphate by fluorimetry.
6. Estimation of sodium/potassium by flame photometry or AAS.
7. Case studies on
    - Total quality management
    - Six sigma
    - Change management/ change control. deviations,
    - Out of specifications (OOS)
    - Out of trend (OOT)
    - Corrective & preventive actions (CAPA)
    - Deviations
8. Development of stability study protocol
9. Estimation of process capability
10. In process and finished product quality control tests for tablets, capsules, parenterals and semisolid dosage forms.
11. Assay of raw materials as per official monographs.
12. Testing of related and foreign substances in drugs and raw materials.
13. To carry out pre formulation study for tablets, parenterals (2 experiments).
14. To study the effect of pH on the solubility of drugs, (1 experiment).
15. Quality control tests for primary and secondary packaging materials.
16. Accelerated stability studies (1 experiment).
17. Improved solubility of drugs using surfactant systems (1 experiment).
18. Improved solubility of drugs using co-solvency method (1 experiment).
19. Determination of Pka and Log p of drugs.

SECOND SEMESTER

HAZARDS AND SAFETY MANAGEMENT
(MQA 201T)

Scope

This course is designed to convey the knowledge necessary to understand issues related to different kinds of hazard and their management. Basic theoretical and practical discussions integrate the proficiency to handle the emergency situation in the pharmaceutical product development process and provides the principle based approach to solve the complex tribulations.

Objectives

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

- Understand about environmental problems among learners.
- Impart basic knowledge about the environment and its allied problems.
- Develop an attitude of concern for the industry environment.
- Ensure safety standards in pharmaceutical industry
- Provide comprehensive knowledge on the safety management.
- Empower ideas to clear mechanism and management in different kinds of hazard management system.
- Teach the method of hazard assessment, procedure, methodology for provide safe industrial atmosphere.

THEORY **60 Hrs**

1. **Multidisciplinary Nature of Environmental Studies:** Natural resources, renewable and non-renewable resources, natural resources and associated problems, **12 Hrs**
   a) Forest resources;
   b) Water resources;
   c) Mineral resources;
   d) Energy resources;
   e) Land resources

   Ecosystems: Concept of an ecosystem and structure and function of an ecosystem. Environmental hazards: Hazards based on air, water, soil and radioisotopes.
2. **Air Based Hazards:** Sources, types of hazards, air circulation maintenance industry for sterile area and non sterile area, preliminary hazard analysis (PHA). Fire protection system: Fire prevention, types of fire extinguishers and critical hazard management system. **12 Hrs**
3. **Chemical Based Hazards:** Sources of chemical hazards, hazards of organic synthesis, sulphonating hazard, organic solvent hazard, control measures for chemical hazards, management of combustible gases, toxic gases and oxygen displacing gases management, regulations for chemical hazard, management of over-exposure to chemicals and TLV concept. **12 Hrs**
4. **Fire and Explosion:** Introduction, industrial processes and hazards potential, mechanical electrical, thermal and process hazards. Safety and hazards regulations. Fire protection system: Fire prevention, types of fire extinguishers and critical hazard management system mechanical and chemical explosion, multiphase reactions, transport effects and global rates. Preventive and protective management from fires and explosion electricity **12 Hrs**

passivation, ventilation, and sprinkling, proofing, relief systems -relief valves, flares, scrubbers.

5. **Hazard and Risk Management:** Self-protective measures against workplace hazards. Critical training for risk management, process of hazard management, ICH guidelines on risk assessment and risk management methods and tools. **12 Hrs**

   Factory act and rules, fundamentals of accident prevention, elements of safety programme and safety management, physicochemical measurements of effluents, BOD, COD, determination of some contaminants, effluent treatment procedure, role of emergency services.

REFERENCES

1. Environmental Science, Y.K. Singh, New Age International Pvt, Publishers, Bangalore.
2. "Quantitative Risk Assessment in Chemical Process Industries" American Institute of Chemical Industries, Centre for Chemical Process safety.
3. The Biodiversity of India, Bharucha Erach, Mapin Pu blishing Pvt. Ltd., Ahmedabad – 380 013, India.
4. Hazardous Chemicals: Safety Management and Global Regulations, T.S.S. Dikshith, CRC Press.

PHARMACEUTICAL VALIDATION
(MQA 202T)

Scope

The main purpose of the subject is to understand about validation and how it can be applied to industry and thus improve the quality of the products. The subject covers the complete information about validation, types, methodology and application.

Objectives

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

- The concepts of calibration, qualification and validation.
- The qualification of various equipments and instruments.
- Process validation of different dosage forms.
- Validation of analytical method for estimation of drugs.
- Cleaning validation of equipments employed in the manufacture of pharmaceuticals.

THEORY **60 Hrs**

1. **Introduction to Validation:** Definition of calibration, qualification and validation, scope, frequency and importance. Difference between calibration and validation. Calibration of weights and measures. Advantages of validation, scope of validation, organization for validation, validation master plan, types of validation, streamlining of qualification & validation process and validation master plan. **10 Hrs**

   Qualification: User requirement specification, design qualification, factory acceptance test (FAT)/site acceptance test (SAT), installation qualification, operational qualification, performance qualification, re-qualification (maintaining status- calibration preventive maintenance, change management).

2. **Qualification of Manufacturing Equipment:** Dry powder mixers, fluid bed and tray dryers, tablet compression (Machine), dry heat sterilization/tunnels, autoclaves, membrane filtration, capsule filling machine. qualification of analytical instruments: UV-Visible spectrophotometer, FTIR, DSC, GC, HPLC, HPTLC, LC-MS. **10 Hrs**

3. **Qualification of Laboratory Equipments:** Hardness tester, friability test apparatus, tap density tester, disintegration tester, dissolution test apparatus. **10 Hrs**

   Validation of utility systems: Pharmaceutical water system &pure steam, HVAC system, compressed air and nitrogen.

4. **Process Validation:** Concept, process and documentation of process validation. Prospective, concurrent & retrospective validation, revalidation criteria, process validation of various formulations (Coated tablets, capsules, ointment/creams, liquid orals and aerosols.), aseptic filling: Media fill validation, USFDA guidelines on process validation- A life cycle approach. **10 Hrs**

   Analytical Method Validation: General principles, validation of analytical method as per ICH guidelines and USP.

5. **Cleaning Validation:** Cleaning method development, validation of analytical method used in cleaning, cleaning of equipment, cleaning of facilities. Cleaning in place (CIP). Validation of facilities in sterile and non-sterile plant. **10 Hrs**

   Computerized System Validation: Electronic records and digital signature - 21 CFR Part 11 and GAMP

6. **General Principles of Intellectual Property:** Concepts of intellectual property (IP), **10 Hrs**

intellectual property protection (IPP), intellectual property rights (IPR), economic importance, mechanism for protection of intellectual property- Patents, copyright, trademark. Factors affecting choice of IP protection; Penalties for violation, role of IP in pharmaceutical industry; global ramification and financial implications. Filing a patent applications, patent application forms and guidelines. Types patent applications-provisional and non provisional, PCT and convention patent applications, international patenting requirement procedures and costs, rights and responsibilities of a patentee, practical aspects regarding maintaining of a patent file, patent infringement meaning and scope. Significance of transfer technology (TOT), IP and ethics-positive and negative aspects of IPP, societal responsibility, avoiding unethical practices.

REFERENCES

1. Pharmaceutical Process Validation, B. T. Loftus & R. A. Nash, Drugs and Pharm Sci. Series, Vol. 129, 3rd Ed., Marcel Dekker Inc., N.Y.
2. The Theory & Practice of Industrial Pharmacy, 3rd edition, Leon Lachman, Herbert A. Lieberman, Joseph. L. Karig, Varghese Publishing House, Bombay.
3. Validation Master Plan by Terveeks or Deeks, Davis Harwood International Publishing.
4. Validation of Aseptic Pharmaceutical Processes, 2nd Edition, by Carleton & Agalloco, (Marcel Dekker).
6. Michael Levin, Pharmaceutical Process Scale-Up", Drugs and Pharm. Sci. Series, Vol. 157,2nd Ed., Marcel Dekker Inc., N.Y.
7. Validation Standard Operating Procedures: A Step by Step Guide for Achieving Compliance in the Pharmaceutical, Medical Device, and Biotech Industries, Syed Imtiaz Haider.
8. Pharmaceutical Equipment Validation: The Ultimate Qualification Handbook, Phillip A. Cloud, Interpharm Press.
9. Validation of Pharmaceutical Processes: Sterile Products, Frederick J. Carlton (Ed.) and James Agalloco (Ed.), Marcel Dekker.
10. Analytical Method validation and Instrument Performance Verification by Churg Chan, Heiman Lam, Y.C. Lee, Yue. Zhang, Wiley Interscience.
11. Validation and Qualification in Analytical Laboratories, Huber L. Informa Healthcare.
12. Validating Corporate Computer Systems: Good IT Practice for Pharmaceutical Manufacturers. Wingate G. Interpharm Press.
13. Validated Cleaning Technologies for Pharmaceutical Manufacturing, LeBlanc DA. Interpharm Press.

AUDITS AND REGULATORY COMPLIANCE
(MPA 203T)

Scope

This course deals with the understanding and process for auditing pharmaceutical industries. This subject covers the methodology involved in the auditing process of different in pharmaceutical industries.

Objectives

Upon completion of this course the student should be able to

- To understand the importance of auditing.
- To understand the methodology of auditing.
- To carry out the audit process.
- To prepare the auditing report.
- To prepare the check list for auditing.

THEORY **60 Hrs**

1. **Introduction:** Objectives, management of audit, responsibilities, planning process, information gathering, administration, classifications of deficiencies. **12 Hrs**
2. **Role of Quality Systems and Audits in Pharmaceutical Manufacturing Environment:** cGMP Regulations, Quality assurance functions, Quality systems approach, Management responsibilities, Resource, Manufacturing operations, Evaluation activities, Transitioning to quality system approach, Audit checklist for drug industries. **12 Hrs**
3. **Auditing of Vendors and Production Department**: Bulk pharmaceutical chemicals and packaging material vendor audit, warehouse and weighing, dry production: Granulation, tableting, coating, capsules, sterile production and packaging. **12 Hrs**
4. **Auditing of Microbiological Laboratory:** Auditing the manufacturing process, product and process information, general areas of interest in the building raw materials, water, packaging materials. **12 Hrs**
5. **Auditing of Quality Assurance and Engineering Department:** Quality assurance maintenance, critical systems: HVAC, water, water for injection systems, ETP. **12 Hrs**

REFERENCES

1. Compliance auditing for Pharmaceutical Manufacturers. Karen Ginsbury and Gil Bismuth,
2. Interpharm/CRC, Boca Raton, London New York,Washington D.C.
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4. Handbook of microbiological Quality control. Rosamund M. Baird, Norman A.Hodges, Stephen P. Denyar. CRC Press. 2000.
5. Laboratory auditing for quality and regulatory compliance. Donald C. Singer, Raluca-loana Stefan, Jacobus F. Van Staden. Taylor and Francis (2005).

PHARMACEUTICAL MANUFACTURING TECHNOLOGY
(MQA 204T)

Scope

This course is designed to impart knowledge and skills necessary to train the students with the industrial activities during Pharmaceutical Manufacturing.

Objectives

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

- The common practice in the pharmaceutical industry developments, plant layout and production planning.
- Will be familiar with the principles and practices of aseptic process technology, non sterile manufacturing technology and packaging technology.
- Have a better understanding of principles and implementation of quality by design (QbD) and process analytical technology (PAT) in pharmaceutical manufacturing.

THEORY **60 Hrs**

1. **Pharmaceutical Industry Developments:** Legal requirements and licenses for API and formulation industry, Plant location-Factors influencing. **12 Hrs**

   Plant Layout: Factors influencing, special provisions, storage space requirements, sterile and aseptic area layout. Production planning: General principles, production systems, calculation of standard cost, process planning, routing, loading, scheduling, dispatching of records, production control.

2. **Aseptic Process Technology:** Manufacturing, manufacturing flowcharts, in process-quality control tests for following sterile dosage forms: Ointment, suspension and emulsion, dry powder, solution (Small volume & large volume). **12 Hrs**

   Advanced Sterile Product Manufacturing Technology: Area planning & environmental control, wall and floor treatment, fixtures and machineries, change rooms, personnel flow, utilities & utilities equipment location, engineering and maintenance. Process Automation in pharmaceutical industry: With specific reference to manufacturing of sterile semisolids, small volume parenterals & large volume parenterals (SVP & LVP), monitoring of parenteral manufacturing facility, cleaning in place (CIP), sterilization in place (SIP), prefilled syringe, powdered jet, needle free injections, and form fill seal technology (FFS).

   Lyophilization Technology: Principles, process, equipment.

3. **Non Sterile Manufacturing Process Technology:** Manufacturing, manufacturing flowcharts, in process-quality control tests for following non-Sterile solid dosage forms: Tablets (Compressed & coated), capsules (Hard & soft). **12 Hrs**

   Advance Non-Sterile Solid Product Manufacturing Technology: Process automation in pharmaceutical industry with specific reference to manufacturing of tablets and coated products, improved tablet production: Tablet production process, granulation and pelletization equipments, continuous and batchmixing, rapid mixing granulators, rota granulators, spheronizers and marumerisers, and other specialized granulation and drying equipments. Problems encountered.

   Coating Technology: Process, equipments, particle coating, fluidized bed coating, and application techniques. Problems encountered.

4. **Containers and Closures for Pharmaceuticals:** Types, performance, assuring quality of **12 Hrs**

glass; types of plastics used, drug plastic interactions, biological tests, modification of plastics by drugs, different types of closures and closure liners, film wrapper, blister packs, bubble packs, shrink packaging, foil /plastic pouches, bottle seals, tape seals, breakable seals and sealed tubes, quality control of packaging material and filling equipment, flexible packaging, product package compatibility, transit worthiness of package, stability aspects of packaging. Evaluation of stability of packaging material.

5. **Quality by Design (Qbd) and Process Analytical Technology (PAT):** Current approach and its limitations. Why QbD is required, advantages, elements of QbD, terminology: QTPP. CMA, CQA, CPP, RLD, design space, design of experiments, risk assessment and mitigation/minimization. Quality by design, formulations by design, QbD for drug products, QbD for drug substances, QbD for excipients, Aanalytical QbD. FDA initiative on process analytical technology. PAT as a driver for improving quality and reducing costs: Quality by design (QbD), QA, QC and GAMP. PAT guidance, standards and regulatory requirements. **12 Hrs**

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2. Sinko PJ. Martin's Physical Pharmacy and Pharmaceutical Sciences, 5th ed., B.I. Publications Pvt. Ltd, Noida, 2006.
3. Pharmaceutical Dosage Forms: Tablets , Lieberman HA, Lachman L, Schwartz JB. Vol. I-III, 2 nd ed., CBS Publishers & distributors, New Delhi, 2005.
4. Modern Pharmaceutics, . Banker GS, Rhodes CT. 4th ed., Marcel Dekker Inc, New York, 2005.
5. Good Manufacturing of Pharmaceuticals (A Plan for total quality control), Sidney H Willing, Murray M, Tuckerman. Williams Hitchings IV, 3rd Edition. Bhalani Publishing House Mumbai.
6. Indian Pharmacopoeia. Controller of Publication. Delhi, 1996.
7. British Pharmacopoeia. British Pharmacopoeia Commission Office, London, 2008.
8. United States Pharmacopoeia. United States Pharmacopeial Convention, Inc, USA, 2003.
9. Pharmaceutical Packaging Technology, Dean D A, Evans E R and Hall I H. London, Taylor & Francis, 1st Edition. UK.
10. Pharmaceutical Packaging Handbook. Edward J Bauer. 2009. Informa Health care USA Inc. New York.
11. Pharmaceutical Manufacturing Handbook. Shaybe Cox Gad. John Willey and Sons, New Jersey, 2008.

QUALITY ASSURANCE PRACTICAL – II PRACTICALS
(MQA 205P)

1. Organic contaminants residue analysis by HPLC.
2. Estimation of Metallic contaminants by flame photometer.
3. Identification of antibiotic residue by TLC.
4. Estimation of hydrogen sulphide in air.
5. Estimation of chlorine in work environment.
6. Sampling and analysis of SO2 using colorimetric method.
7. Qualification of following pharma equipment.
   a. Autoclave.
   b. Hot air oven.
   c. Powder mixer (Dry).
   d. Tablet compression machine.
8. Validation of an analytical method for a drug.
9. Validation of a processing area.
10. Qualification of at least two analytical instruments.
11. Cleaning validation of one equipment.
12. Qualification of pharmaceutical testing equipment (Dissolution testing apparatus, friability apparatus, disintegration tester).
13. Check list for bulk pharmaceutical chemicals vendors.
14. Check list for tableting production.
15. Check list for sterile production area.
16. Check list for Water for injection.
17. Design of plant layout: Sterile and non-sterile.
18. Case study on application of QbD.
19. Case study on application of PAT.