GOA UNIVERSITY

P.O TALEIGAO PLATEAU

GOA – 403 206

SYLLABUS FOR M. PHARM (QUALITY ASSURANCE)

APPROVED BY THE BOARD OF STUDIES

FOR THE ACADEMIC YEAR

PURPOSE

To train a Pharmacist who shall:

- Display talent and competence, backed by reasoning ability to achieve standards in manufacture of quality products in pharmaceutical industry and to lead a company towards achieving global standards through proper in process standards.
- Exercise a sense of power and confidence to focus attention on irregularities, errors, exceptions and deviations from standards.
- Articulate a compelling vision to the future by encouraging and implementing ideas, procedures and techniques by thinking out of the box.

PRE-REQUISITES

A candidate who has passed the B. Pharm. Examination of Goa University or an examination of any other Indian University recognized as equivalent thereto with at least **50%** marks in aggregate in one and the same sitting and with **GPAT** be admitted to the M. Pharm. Course (partly by papers and partly by thesis) in one of the specialisation of Pharmacy mentioned below in which he registers as a post-graduate student. However, if the **GPAT** candidates are not available then the vacant seats shall be filled by admitting the candidates without **GPAT** but who have passed the **B. Pharm**. Examination with at least **50%** marks in aggregate in one and the same sitting.

TABLE OF CONTENTS

M. Pharm. (Quality Assurance)

Semester I

Semester II

SEMESTER - I

Analytical Techniques

72 hr

No	Topics	Duration
I	**Separation Techniques:**	
1	**Classification of chromatographic methods** based on mechanism of separation & their basic principles including Ion exchange and separation of chiral compounds.	2
2	**Gas Chromatography:** Instrumentation, column efficiency parameters, derivatisation methods, application in pharmaceutical analysis, validation of analytical method	6
3	**Liquid Chromatography:** Instrumentation in HPLC, UPLC, Comparison of GC & HPLC, phase packing materials, column selection, mobile phase selection, efficiency parameters, application in pharmaceutical analysis including validation of analytical method.	6
4	**HPTLC:** Instrumentation & pharmaceutical applications of HPTLC Advanced techniques: Flash chromatography, Supercritical Fluid chromatography, Capillary Electrophoresis (CE), Ion chromatography	3 4
II	**Spectroscopic Methods:**	
1	**UV- Visible spectroscopy:** Introduction, Basic principles, Applications; Absorption spectra of organic compounds & complexes illustrating the phenomenon & its utilization in qualitative & quantitative studies of drugs; calculation of absorption maximum of unsaturated hydrocarbons- Woodwards-Fieser Rule, Derivative spectroscopy, Derivation of equation for Simultaneous determination and Absorbance Ratio methods, Application of Chemometrics.	4
2	**IR Spectroscopy:** Interaction of infrared radiation with organic molecules & its effect on bonds; Sample handling, detailed interpretation of ir spectra, Pharmacopoeial Importance of IR spectra. Instrumentation in Brief, Dispersive IR spectrophotometer compared with FTIR and ATR, NIR Raman Spectroscopy	4 1 10
3	**NMR Spectroscopy:** Fundamental principles of NMR, Concept of Chemical shift, Spin-spin coupling, Decoupling techniques and their importance, shielding &deshielding; solvents in pmr and ^{13}C-NMR; Detailed interpretation studies of pmr spectra; Introduction & application of ^{13}C-NMR spectra and 2D NMR.	2

4	Instrumentation in Brief, FTNMR. **Mass Spectroscopy:** Basic principles Ionization techniques, mass spectrum & its characteristics - molecular ion, metastable ion, fragment ions, isotope ions; fragmentation process and rules & characteristic fragmentation patterns, fragment characteristics in relation to parent structure & functional groups; relative abundance of isotopes & their contribution to characteristic peaks. Mass spectroscopy in Metabolomics Instrumentation- Mass spectrometers, Tandem mass spectrometers Hyphenated instruments – LCMS, GCMS	7 3
III	**<u>Other Techniques and Applications</u>:**	
1	**Thermal Analysis:** Theory, instrumentation & applications of Thermo-gravimetric analysis,differential thermal analysis, differential scanning calorimeter.	6
2	**Immunochemical Techniques:** Immuno-electrophoresis, Immuno-precipitation, ELISA, Radioimmunoassay.	4
3	**Powder X-ray Diffraction:** Braggs law and its applications,Instrumentation and pharmaceutical applications.	4
4	**Impurity Profiling**	6

Analytical Techniques
(Practicals)

*A minimum of 18 Practical's (Exercises on both Quantitaive, Qualitative analysis to be elaborated) shall be conducted from the following.

Practical-1
UV/Visible spectrum scanning of a few organic compounds for UV- absorption and correlations of structures and isosbestic point in case of mixtures.

Practical-2 to 3
Effect of solvents and pH on UV spectrum of drugs
Determination of Rate constant by UV spectroscopy

Practical-4 to 8
Estimation of multi component formulation by UV- Spectrophotometer in formulations (Simultaneous equation Method, Absorbance Ratio Method)

Practical-8 to 9
Experiments based on the application of derivative spectroscopy.

Practical-10 to 11
Experiments based on HPLC (Isocratic and Gradient elution) techniques.

- Single and multiple component analysis
- Calculation of System Suitability Parameters

Practical-12 to 14
Interpretation of drugs by IR spectra – Use pharmacopoeial spectra (atleast 10) for correlation of structural features

Practical- 15 to 19
Problems Solving: (UV, IR, NMR, Mass) structural elucidation of atleast 10 compounds with UV, IR, NMR and Mass spectral data.

Practical-20
Separation of protein drug substances by electrophoresis

Practical -21
Impurity profiling – Characterization and determination techniques – TLC, IR spctroscopy, UV spectrometry

Practical -22
Study and interpreting X-Ray Diffraction patterns for study of polymorphic forms of compounds.

Practical -23
Study of DSC thermograms for various interactions between compounds

BOOKS RECOMMENDED:

1. Skoog, DA, Holler, FJ, Crouch, SR. Principles of instrumental analysis.6thed., Baba BarkhaNath printers,
Haryana, 2007
2. Silverstein, RM, Webstar, FX. Spectrometric identification of organic compounds. 6th ed., John Wiley & Sons (Asia) Pvt. Ltd., Singapore, 2005
3. William Kemp. Organic spectroscopy, 3rded., Palgrave, New York, 2006
4. Jag Mohan, Organic spectroscopy: Principles and Applications, 2nded.,Narosa publishing housePvt Ltd., New Delhi, 2005
5. Conners KA. A Text book of pharmaceutical analysis, 3rd ed., John Wiley & Sons, Singapore,2004
6. Willard HH, Merritt LL, Dean JA, Settle FA. Instrumental methods of analysis, 7th ed., CBS Publishers & Distributors, New Delhi, 1986
7. Pavia DL, Lampman GM, Kriz GS, Vyvyan JA. Introduction to spectroscopy. 4th ed., Brookescolepublishers, California, 2008
8. Sharma BK. Instrumental methods of chemical analysis, 25th Ed., Goel Publishing house, Meerut, 2006
9. Beckett, AH, Stenlake, JB. Practical pharmaceutical chemistry, Part I & II, 4th ed., CBS Publishers & distributors, New Delhi, 2004
10. Ewing, GW. Instrumental methods of chemical analysis, 5thed., McGraw Hill Book Company, New York, 1985
11. Schirmer, RE. Modem methods of pharmaceutical analysis, Vol. I & II, 2nded., CRC Press, Florida, 2000

12. Moffat, AC, Osselton, MC, Widdop, B. Clarke's analysis of drugs and poisons, Vol. I & II, 3rd ed., K.M. Varghese Company, Mumbai, 2004

Product Development –I

72Hours

No	Topics	Duration
1	Introduction and Perspective Framework for product development.	1
2	Preformulation Studies Protocol, Physical-Chemical-Biological Characterization, Fundamental – Derived Properties, size-size distribution, surface area, crystal morphology-properties & influence, Solubility & pH solubility profile, Partition coefficient, pKa, drug permeation, dissolution, compatibility studies.	12
3	Solubilization Techniques Formulation of poorly soluble drugs.	3
4	Drug Stability Solid state, solution phase physical stability testing, Stability testing general protocol, reference to regulatory requirements, WHO, USFDA, ICH guidelines [Q1A (R2), Q1B, Q1C, Q1D, Q1E, Q1F, Q5C], Kinetic principles applied for stability evaluation and their applications in predicting shelf life, accelerated stability study & shelf life assignment	8
5	Tablet Technology Formulation, manufacturing & evaluation, emphasis on unit processes, granulation technology, physics of tablet- compression & compression tooling, Advanced granulation techniques & multi process equipments- single pot, FBP etc.	8
6	Coating of solids & solid dosage forms: Tablet film coating, Aqueous & Non-aqueous systems, polymers, mechanism film formation, auto coating equipments Accela cota, Dria-coater, Glatt coater, Freund Hi coater etc., ancillary devices & gadgets including metering equipment, evaluation, film coating defects, particulate coating methods, extrusion, spheronization, pelletization etc.	8
7	Capsulation Technology Empty capsules, Gelatin, physical-chemical properties, formulation & manufacture of Hard Capsules, fill principles- equipments –a review, semisolids, liquids as fill material.	8

8	Liquid dosage forms Monophasic, biphasic, formulation development & evaluation, processing & equipments, Microemulsions	8
9	Parenteral Technology Formulation review, small volume, large volume, manufacturing facility-design considerations, environmental controls, processing, dry powder injectables- freeze drying	8
10	Packaging development: Types of packages, Flexible packaging, primary, secondary & tertiary, quality evaluation as applicable to packages, Child resistant, tamper evident, advancement in packaging.	8

BOOKS RECOMMENDED: -

1. Drug Stability, J.T. Carstensen, Marcel Dekker, New York.
2. Chemical Stability of Pharmaceuticals-A Handbook for Pharmacists, Kenneth Connors, John Wiley and Sons, Inc.
3. Lachmann, L., Lieberman, H.A. & Kanig, J.I.: The Theory and Practice of Industrial pharmacy. Lea and Fibiger, Philadelphia.
4. Banker, G.S. & Rhodes, C.T. : Modern Pharmaceutics, Marcel Dekker Inc. New York and Basel.
5. Turco, S. & King R.E. : Sterile Dosage Forms, Lea and Febiger, Philadelphia
6. Bean, H.S., Backett, A.H. & Carless, J.E: Advances in Pharmaceutical Sciences, Academic Press, London and New york.
7. Jain, N.K.: Controlled and Novel Drug Delivery , CBS, Delhi
8. Jain N. K. Pharmaceutical Product Development, CBS Publisher, Delhi

Product Development –I

(PRACTICALS)

Experiments based on following concepts:

1. Formulation of compressed tablets (Antipyretic drug).
2. Evaluation of compressed tablets (Antipyretic drug).
3. Formulation of topical preparations (Cream & Gel) (Anti-inflammatory drug).
4. Evaluation of topical preparations (Cream & Gel) (Anti-inflammatory drug).
5. Formulation of oral liquids (Anti-histaminic & Expectorant).
6. Evaluation of oral liquids (Anti-histaminic & Expectorant).
7. Formulation of stable suspensions (Antacid).
8. Evaluation of stable suspensions (Antacid).
9. Formulation of dry suspensions (Antibiotics).
10. Evaluation of dry suspensions (Antibiotics).
11. Formulation of emulsions (Liquid Paraffin & Magnesium Hydroxide).
12. Evaluation of emulsions (Liquid Paraffin & Magnesium Hydroxide).
13. Formulation of small volume parenterals (Ascorbic Acid).
14. Evaluation of small volume parenterals (Ascorbic Acid).
15. Formulation of Injectable/ophthalmic preparations (Pilocarpin/ Antiglaucoma).
16. Evaluation of Injectable/ophthalmic preparations (Pilocarpin/ Antiglaucoma).
17. Assessment of stability studies according to ICH guidelines (Aspirin)
18. Evaluation of packaging materials (Carton/ Paperboard).

BOOKS RECOMMENDED:

1. Drug Stability, J.T. Carstensen, Marcel Dekker, New York.
2. Chemical Stability of Pharmaceuticals-A Handbook for Pharmacists, Kenneth Connors, John Wiley and Sons, Inc.
3. Lachmann, L., Lieberman, H.A. & Kanig, J.I.: The Theory and Practice of Industrial pharmacy. Lea and Fibiger, Philadelphia.
4. Banker, G.S. & Rhodes, C.T. : Modern Pharmaceutics, Marcel Dekker Inc. New York and Basel.
5. Turco, S. & King R.E. : Sterile Dosage Forms, Lea and Febiger, Philadelphia
6. Bean, H.S., Backett, A.H. & Carless, J.E: Advances in Pharmaceutical Sciences, Academic Press, London and New york.
7. Jain, N.K.: Controlled and Novel Drug Delivery , CBS, Delhi
8. Jain N. K. Pharmaceutical Product Development, CBS Publisher, Delhi

QUALITY MANAGEMENT – I

72Hours

No	Topics	Duration
1.	Total Quality Management and its importance to improve business performance. Quality Models in business, Six Sigma Concept, Six Sigma tools, Continuous improvements and its applications, Lean Concept for Process improvements	6
2.	Integrated Management Systems. Assessing effectiveness of Management systems.	2
3.	Management and Planning tools : Affinity diagram, Prioritization matrix	2
4.	ISO 9001/ ISO 13485 standards and its implementation	4
5.	Change Controls: Types of change controls, Handling of change controls, Personnel to be involved, Impact assessments.	2
6.	Incident Handling and Deviations	2
7.	Corrective Actions and Preventive Actions	2
8.	Personnel Training and its Evaluation, Development of Job responsibilities, Competency matrix	4
9.	Environmental monitoring, setting of limits and its evaluation. Control of contamination and cross contamination.	8
10.	Quality Related Guidelines, Legislations and Regulations: Schedule M, 21CFR Part 210, 211 and 820, PIC guidelines for GMP, Schedule L1, EU guidelines for GMP, WHO GMP guidelines, Canadian GMP Guidelines,	12
11.	Designing of Manufacturing facilities for Excipients, API, Drug Formulations, Medical Devices. ISPE Baseline guidelines. Designing requirements for HVAC systems. ISPE guidelines, WHO guidelines. Designing requirements for Water systems. ISPE guidelines, USFDA guidelines, WHO Guidelines	8
12.	Risk Analysis: ICH Q9, HACCP, FMEA	2
13.	Quality Planning in Product Life cycle. Product Quality Life cycle implementation (PQLI). ISPE guideline.	2
14.	Process mapping and determining critical control points	2
15.	Control on starting materials, Vendor approval and monitoring	2
16.	In- process quality control on various dosage forms- Sterile and non sterile.	2
17.	Control on Finished Products. Regulatory requirements by different countries.	2
18.	Packaging and labeling controls,	2

	Line clearances	

Books Recommended

1. Drugs & Cosmetics Act 1940 and rules there under.
2. Drugs Laws by Hussain.
3. Indian Patent Act.
4. Quality assurance & GLP by Y. Anjaneyulu.
5. Quality control & Application by Bentrand L. Hanser.
6. Guidelines of various countries like MCA, TGA, ICH.
7. GLP regulation by Alen Hirsch Vol 38 Marcel Decker series
8. GMP for pharmaceuticals forth edition by S. Willing, J. Stocker Marcel Decker series 1997.
9. I.P., B.P., U.S.P. International Pharmacopoeia

VALIDATION

72 Hours

No	Topics	Duration
1	Introduction to Pharmaceutical validation definition, scope of validation, manufacturing process model, advantage of validation, organization for validation, Validation Master Plan, User Requirement Specifications Technical Specifications, Design qualification, Factory Acceptance Tests, Site Acceptance Tests, Installation qualification, Operational qualification, Performance qualification. Requalification	**15**
2	Calibration of instruments. Regulatory Requirements.	**4**
3	Area Qualification, Preparation of Protocols, Execution of Qualification Activity, Preparation of reports, Handling of Deviations.	**4**
4	HVAC System Qualification / Validation Preparation of Protocols, Execution of Qualification Activity, Preparation of reports, Handling of Deviations / Excursions.	**4**
5	Water System Qualification / Validation Preparation of Protocols, Execution of Qualification Activity, Preparation of reports, Handling of Deviations.	**4**
6	Equipment Qualifications, Preparation of Protocols, Execution of Qualification Activity, Preparation of reports, Handling of Deviations.	**4**
7	Qualification of Compressed Air System, Preparation of Protocols, Execution of Qualification Activity, Preparation of reports, Handling of Deviations.	**4**
8	Qualification of Pure Steam Generator Preparation of Protocols,	**4**

	Execution of Qualification Activity, Preparation of reports, Handling of Deviations.	
9	Performance Qualification of Sterilizing Equipment. Performance Qualification of Steam Sterilizers, Dry heat sterilizers, Dry heat sterilizer tunnels, ETO sterilizers and Gamma radiation sterilizers.	**4**
10	Process validation: prospective, concurrent, retrospective and revalidation. Process Validation of Tablets manufacturing, Process Validation of Liquid Orals Process Validation of Capsules Process Validation of Non-Sterile semisolids Process Validation of Aerosols Process validation of Sterile Products, Media Fills	**10**
11	Cleaning Validation, Equipment and Area cleaning and monitoring. Disinfectant Efficacy Testing	**4**
12	Computer system Validation, GAMP Guidelines, 21CFR Part 11	**2**
13	Packaging Process validation	**2**
14	Analytical Method Validations, Analytical Method Transfers, Direct Transfers and Indirect Transfers. Microbiological Method Validations.	**4**
15	Product Transfers from Development lab, Site transfers of Products.	**2**
16	Process Analytical Technology (PAT). USFDA Guidelines	**2**

BOOKS RECOMMENDED

- Pharmaceutical Process Validation, B. T. Loftus and R. A. Nash, Drugs and Pharm Sci. Series, Vol. 129, Marcel Dekker Inc., New York.
- Validation of Aseptic Pharmaceutical Processes, Carleton and Agalloco, Marcel Dekker Inc., New York.
- Cleaning Validation Manual: A Comprehensive Guide for the Pharmaceutical and Biotechnology Industries by Syed Imtiaz Haider and Erfan Syed Asif
- Pharmaceutical Computer Systems Validation: Quality Assurance, Risk Management and Regulatory Compliance, Second Edition by Guy Wingate
- Pharmaceutical Process Scale-Up", Michael Levin, Drugs and Pharm. Sci. Series, Vol. 157, Marcel Dekker Inc., New York.
- Pharmaceutical Process Validation – Robert A. Nash, Alfred H. Wachter
- Process Validation in manufacturing of biopharmaceuticals: Guidelines – Anurag Singh Rathore, Gail Sofer, G. K. Sofer
- Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials (v. 1) by WHO

SEMESTER II

PRODUCT DEVELOPMENT – II

72 Hours

No	Topics	Duration
1	DISSOLUTION TECHNOLOGY Dissolution testing devices viz forced convection, non sink and sink devices, continuous flow through methods, effect of environmental factors during dissolution testing, dissolution test apparatus official-USP 1 to 7, Disso testing of suspensions, topical and transdermal products, suppositories and controlled release products, recommended apparatus, in-vitro in-vivo correlations	6
2	CONCEPTS AND SYSTEMS DESIGN FOR RATE CONTROLLED DELIVERY Rate pre-programmed, activation modulated and feed back regulated drug delivery systems. Effect of system parameters on controlled release drug delivery	6
3	ORAL DRUG DELIVERY SYSTEMS Osmotic pressure controlled, membrane permeation controlled, pH controlled, Ion-exchange controlled, gel diffusion controlled and hydro dynamically balanced systems, modulation of gastro intestinal transit time-Gastro retentive	6
4	MUCOSAL DRUG DELIVERY SYSTEMS Mechanism of transmucosal permeation and mucosal membrane models, Buccal, Nasal, pulmonary, rectal and vaginal drug delivery systems, delivery of peptide based pharmaceutical.	8
5	OCULAR DELIVERY OF DRUGS Ocular delivery of drugs-constraints, development of ocular controlled release therapeutic systems including sol-gel & gel-sol phase transition systems.	6
6	TRANSDERMAL DRUG DELIVERY Permeation through skin, mechanistic analysis, permeation enhancers, technologies for developing transdermal drug delivery systems, gels, patches and evaluation there of.	6
7	PARENTERAL DRUG DELIVERY SYSTEMS Injectable controlled released formulations, long acting contraceptive formulations, implantable drug delivery systems.	6
8	INTRAVAGINAL / INTRAUTERINE DRUG DELIVERY SYSTEMS Design of devices, rational in design, Medicated IUDS, copper IUD, Homone releasing IUD.	6
9	SITE SPECIFIC DRUG DELIVERY Active and passive targeting, monoclonal antibiodies for drug targeting,	6

	particulate carrier systems, microspheres, Liposomes, Niosomes.	
10	NANOTECHNOLOGY AND NANOMEDICINES : Insight of Nanoparticulate drug delivery systems ,Fundamentals of Drug Nanoparticles, Manufacturing of Nanoparticles – Milling, Homogenization , Supercritical fluid Technology, Emulsion process, Characterization of Nanoparticles, Drug delivery applications of Nanoparticles, Clinical, Ethical & Regulatory issues.	6
11	CHRONOPHARMACEUTICAL DRUG DELIVERY SYSTEM Introduction and basis of drug delivery. Approaches and Classification of Chronopharmaceutical DDS. Chronogenetics, Chronopharmacokinetics, Chronotherapy CR systems triggered by physical and/or chemical activation, Chronopharmacodynamics, chronomics.	4
12	DRUG APPROVAL AND PREPARATION OF DOCUMENTS.	2
13	Quality by Design, Formulations by Design, QbD for drug products, QbD for Drug Substances, QbD for Excipients, Analytical QbD.	4

Recommended Books

- P. Tyle and B. Ram, Targeted Therapeutic Systems, Marcel Dekker, N.Y., 1990.
- N.K. Jain, Advances in Controlled and novel drug delivery, 2001, CBS, New Delhi.
- Advanced Pharmaceutical Solids, Jens T Carstenson, Taylor & Francis.
- J. R. Robinson & V.H.L. Lee (Eds), Controlled Drug Delivery, Fundamentals and applications, Vol 29 &Vol 31, 2nd Edition, Marcel Dekker, N.Y. 1987
- International Journal of Pharmaceutical Sciences and Nanotechnology
- Encyclopedia of Nanoscience and Nanotechnology (New 15-Volume Set)
- Nanomedicine and Nanobiotechnology Editor- Logothetidis, Stergios
- Chronopharmaceutics: Science and Technology for Biological Rhythm Guided Therapy and Prevention of Diseases By Bi-Botti C. Youan
- J.T. Carstensen, Drug Stability: Principles and Practices, Marcel Dekker, N.Y.
- N.K. Jain, Pharmaceutical product development. CBS publication and distributors, New Delhi.
- Novel drug delivery systems by Chien
- Oral mucosal drug delivery by M J Rathbone
- G.S. Banker and C.T.Rhodes, Modern Pharmaceutics, IInd edition, Marcel Dekker, INC, NewYork.
- Specialized drug delivery systems by Praveen Tyle.
- USP

- Pharmaceutical Dissolution Testing By Umesh Bankar

Product Development II

Practical

1. Preparation of a SOLID DISPERSION - two methods (Anti- inflammatory).
2. Evaluation of a SOLID DISPERSION - two methods (Anti- inflammatory).
3. Preparation of a Transdermal patch (Analgesic/ Antidiabetic).
4. Evaluation of a Transdermal patch (Analgesic/ Antidiabetic).
5. Preparation of a topical Gel (Anti-inflammatory).
6. Evaluation of a topical Gel (Anti-inflammatory).
7. Preparation of matrix SR Tablets (Antidiabetic).
8. Evaluation of matrix SR Tablets (Antidiabetic).
9. Preparation of Gastro Retentive Drug delivery System (Antacid).
10. Evaluation of Gastro Retentive Drug delivery System (Antacid).
11. Preparation of Microspheres (Antibacterial/Antifungal).
12. Evaluation of Microspheres (Antibacterial/Antifungal).
13. Preparation of a hydrodynamically balanced drug delivery system (Antibiotics).
14. Evaluation of a hydrodynamically balanced drug delivery system (Antibiotics).
15. Preparation of Buccal Patches (Analgesic/ Anti-inflammatory).
16. Evaluation of Buccal Patches (Analgesic/ Anti-inflammatory).

QUALITY MANAGEMENT – II

72 Hours

No	Topics	Duration
1	Quality control laboratory: Design of QC laboratory for chemical, instrumental and microbiological analysis. Good Practices in QC laboratory, Schedule L1, standardization of reagents, labeling of reagents, control samples, controls on animal house, data generation and storage, QC documentation, LIMS	**10**
2	Sampling Techniques, Sampling Plans	**2**
3	Stability Studies, ICH Guidelines, WHO Guidelines	**4**
4	Out of Trend and Out of specification handling and evaluation. OOS Guidelines of USFDA.	**2**
5	Good warehousing practices. Pest and rodent controls. Temperature mapping and monitoring of warehouses.	**6**
6	Good Distribution Practices	**6**
7	Annual Product reviews	**4**
8	Waste disposal, disposal procedures and records, current regulations for waste disposal.	**4**
9	Contract manufacturing and analysis	**4**
10	Consumer Protection Act Environment Protection Act Factories Act Packaged commodities Act	**10**
11	Import/Export policy. Requirements for import and export of Excipients, Drug substances and Drug Products / Devices.	**2**
12	Present status and scope of Pharmaceutical industry in India.	**2**

13	Analytical Method Transfers.	**2**
14	Complaints handling. Root cause analysis. Keppener Trego technique for investigations. Six sigma tools, SQC tools, Impact assessment, Establishment of CAPA. Handling of Recall and recall procedures. Mock recalls.	**6**

Recommended Books:

1. Drugs & Cosmetics Act 1940 and rules there under.

2. Drugs Laws by Hussain.

3. Indian Patent Act.

4. Quality assurance & GLP by Y. Anjaneyulu.

5. Quality control & Application by Bentrand L. Hanser.

6. Guidelines of various countries like MCA, TGA, ICH.

7. GLP regulation by Alen Hirsch Vol 38 Marcel Decker series

8. GMP for pharmaceuticals forth edition by S. Willing, J. Stocker Marcel Decker series 1997.

9. I.P., B.P., U.S.P. International Pharmacopoeia

RESEARCH METHODOLOGY

72Hours

No	Topics	Duration
I	**Research Methodology**	
1	*Introduction:* Meaning of research, purpose of research and types of research (clinical experimental, basic, applied and patent and oriented research), Approaches to research, Criteria for good research, qualitative & quantitative research methods.	3
2	*Literature survey:* Using library, book and journals, MEDLINE- internet getting patents and reprints of articles as sources for literature survey	1
3	*Research report/paper writing/thesis writing / poster presentation:* Different parts of research report or paper Title-title of project with authors name Abstract-statement of the problem, background list in brief, purpose and scope, Key words , Methodology-subject, apparatus/instrumentation and procedure. Results-tables, graphs, figures and statistical presentation Discussion-support or non-support to hypothesis. Practical and theoretical implications. Acknowledgements, References , Errata , Importance of spell check, Use of foot notes, Bibliography.	3
4	*Methods and tools used in research:* Selection of research problem, research design; meaning, concept & features of research design, experimental design, plan of research work. Qualitative studies, quantitative studies. Simple data organization, descriptive data organization. Limitations and sources of errors. Enquiries in forms of questionnaire, opinionnaire and interviews Simple data organization, descriptive data organization. Limitations and sources of errors. Enquiries in forms of questionnaire, opinionnaire and interviews	6
II	**Statistics and Computer Applications**	
1	Introduction, Concept of Statistics in Quality Control (SQC), its role and uses. Collection, organization, measurement of central tendencies & dispersion; degree of freedom, standard deviation, standard error, Coefficient of variation, Probability, Sample and Sampling method.	**5**

	Process capability study. Statistical process control Charts.	
2	**Estimation and Hypothesis testing:** Null Hypothesis, confidence level, Point & interval estimation, concept of hypothesis testing & types of error, Student 't' test, Chi-Square test	**5**
3	**Linear regression and Correlation:** Analysis of variance (one way & two way), Factorial design	**3**
4	Brief review of non parametric tests, experimental design in clinical trials, statistical test for bioequivalence, Dose-Response study, statistical quality control; validation, optimization techniques & screening design, significance of coefficient of correlation, non-linear regression, Application of software for statistical calculations.	**10**
III	**Biological Evaluation**	
1	Biological Evaluation and Standardization – Need for biological models and methodologies	**2**
2	Biological Standardization: General Principles, Scope & limitations of Bioassays. Bio- assays of some Official Drugs.	**2**
3	Sterility Tests: Methodology & Interpretation.	**4**
4	Microbiological Limit Tests, Tests for effectiveness of antimicrobial preservatives.	**2**
5	Radio immunoassay: General principles, scope and limitations, radio immunoassay of some drugs like insulin, digitalis etc.	**4**
6	Laboratory Animals a) Commonly used laboratory, transgenic and other genetically prone animal models (viz. nude mice SH rats etc.) b) Techniques of blood collection, anesthesia & euthanasia of experiment animals. c) Maintenance & breeding of laboratory animals. d) Regulation and ethics requirements. e) Guidelines & regulatory agencies – CPCSEA, OECD, FDA ICH, FHSA, EPA, EEC, WHO, etc. f) Importance of alternative experimental models, its advantages & disadvantages g) Cell lines, for drug screening	**6**
7	Preclinical Drug Evaluation, acute, sub acute and chronic toxicity studies, LD50 & ED50 determination, evaluation of compound for its biological activity, study of special toxicities like teratogenicity and mutagenicity.	**5**

8	Pyrogens- Source of contamination, chemistry and properties of bacterial pyrogens and endotoxins, Mechanism of action of pyrogens, Pharmaceutical aspects, Pyrogen test of IP compared to that of BP & USP, Interpretation of data, Comparison of LAL &official pyrogen tests.	**4**
9	Clinical trials: definition, phase I – IV studies, design documentation, presentation and interpretation, statistical analysis of clinical data, factorial design, guidelines as per Indian and other regulatory authorities.	**5**

RESEARCH METHODOLOGY

PRACTICALS

1. Sterility testing of devices/sterile products/immunological products.
2. Pyrogen testing.
3. Microbiological limit test on excipients/non sterile products.
4. LD 50 and ED 50 determination.
5. Eye irritation and Patch test.
6. Bioassays of some drugs including microbiological.
7. Test for effectiveness of preservatives, USP.
8. Demonstration of statistical softwares as applicable.

BOOKS RECOMMENDED:

(1) Research in education – John W. Best Jems V. Kahn
(2) Research methodology – C. R. Kothari
(3) Methodology and techniques of social research – Willkinson and Bhandarkar
(4) Presentation skills – Michel Halton – Indian society for institute education
(5) Practical introduction to copyrights – Gavin Mofariane
(6) Thesis projects in sciences and engineering – Richard M. Devis
(7) Scientist in legal system – Ann Labor Science
(8) Thesis and assessment writing – Janolthon Anderson
(9) Writing a technical paper – Donald Manzel
(10)Effective business report writing – Lel and Brown
(11)Protection of industrial property rights – Purshottam Das and Gokul Das
(12)Spelling for millions – Edna Furmess
(13)Preparation for publications – King Edwards hospital foundation for London
(14)How to write and publish a scientific paper – Robert A. Day Cambridge University Press 4th Edition, 1994
(15)Introduction to Statistical Methods- C. B. Gupta
(16)A first course in Mathematical Statistics- C. E. Weatherborn
(17)Introduction to Biostatistics-Mahajan
(18)Experimental Pharmacology by S K Kulkarni.
(19)Fundamentals of Science & Technology Communication – N R Rajagopal, NISCAIR (CSIR)

DOCUMENTATION & QUALITY AUDITS

- **Expertise from Industry to be invited**

72 Hours

No	Topics	Duration
1	Documentation Requirements of Schedule M, WHO GMP Guidelines, 21 CFR Part 820, 21 CFR Part 210 & 211, PIC GMP Guidelines, ISO 9001, ISO 13485	**6**
2	Good Documentation Practices, Format Controls	**5**
3	Documents & Records: Log Books, Master Formulas Batch Manufacturing Records Cleaning & Disinfection records Training Records Approvals, Control, retention and disposal of documents and records.	**8**
4	Standard Operating Procedures, Establishment, Approvals, Control, distribution, review & revisions,	**6**
5	Distribution records, Schedule U	**4**
6	Design and Development Design Control Implementation, design controls for manufacturers, Design control procedures and implementation, Design control audits, Design development plan, Design control project management, DMR (device master record)	**6**
7	Electronic Data Management System	**5**
8	Risk management and mapping: Assessment & evaluation of the biological look at predicates, materials, processes, and composites to inform of biological and toxicological hazards and regulatory implications, known and potential. Recommended ways to mitigate risk, [whether through testing or by establishing the safety of the materials and processes]. **Risk analysis:** Failure modes and effects analysis (FMEA), Fault tree analysis (FTA), Preliminary hazard analysis (PHA), Health hazard evaluation (HHE). **Test Planning:** know the tests needed before beginning with device development. Present a testing road map that facilitates planning, and budgeting.	**8**

	Reality Check: evaluate the necessity and appropriateness of test plans and offer options or recommendations. **Crisis Support:** Either before or after you receive notification of an FDA inspection, or are issued a 483, or a warning letter, preparation or development of an effective response.	
9	Document administrator and control	**4**
10	Documentation involved in validation and qualification process	**4**
11	Documentation of manufacturing processes.	**4**
12	Audits and Self Inspection: Types of audits Systems audit, Product audit, Process audit, Audit of Drug Product manufacturing facility Audit of Drug substance manufacturing facility and ICH Q7 Audit of Excipients manufacturing facility and IPEC guidelines Audit of Packaging material manufacturing facility Audit report preparation Internal audits, Facing external audits Audit Compliance report	**12**

BOOKS RECOMMENDED

- Juran's Quality Handbook, 5th Ed, by J M Juran, A B Godfrey, McGrawHill International Edition
- ISO 9001 and Total Quality Management – Sadhank. G. Ghosh.
- A guide to Total Quality Management – KaushikMaitra and SedhanK.Ghosh.
- 14. ICH Guidelines, OECD Guidelines, 21 CFR Guidelines, MHRA Guidelines, WHO
- Guidelines, D & C Act, DPCO Act
- United States Pharmacopoeia, USP Convention Inc.
- ISO 9000 Quality Systems Handbook - updated for the ISO 9001:2008 standard, Sixth Edition: Using the standards as a framework for business improvement by David Hoyle