PAPER II: PREFORMULATION AND PRODUCTION MANAGEMENT

GOAL: To train the students to be on par with the routine of Industrial activities in R&D, F&D, IPR, RA and Production

OBJECTIVES: The candidates shall be able to:

- Confidently handle the scheduled activities in a Pharmaceutical firm.
- Manage the production of large batches of pharmaceutical formulations.
- Assist in Regulatory Audit process.
- To establish safety guidelines, which prevent industrial hazards.

COURSE DESCRIPTION

THEORY **50 Hours (T:2Hours/Week)**

1. **PREFORMULATION STUDIES** **06 Hrs.**

(Marks allotment : 15)

Introduction, Consideration of physico-chemical properties of new drug molecules for different dosage forms. Aqueous solubility, organic solubility, intrinsic solubility, methods of enhancement of solubility-surfactants, pH, co-solvency, solid dispersion, complexation. Techniques for the study of crystal properties and polymorphism - DSC, TGA, PXRD, Optical microscopy, hot stage microscopy. Excipient compatibility studies, Preformulation stability studies.

2. **COMPACTION, COMPRESSION, AND CONSOLIDATION** **05 Hrs.**

(Marks allotment : 15)

Compression, consolidation, decompression, compaction of powders with a particular reference to distribution and measurement of forces within the powder mass undergoing compression. Influence of compression force on the properties of tablets. Effect of particle size, moisture content, lubrication etc. on strength of tablets. A brief study on formulation aspects of tablets such as mouth dissolving tablets, dispersible tablets, chewable tablets and medicated lozenges.

3. QUALITY BY DESIGN, DESIGN OF EXPERIMENTS, FORMULATION BY DESIGN **04 Hrs.**

(Marks allotment : 10)

USFDA's view of QbD, Elements of QbD, QbD tools, Design of experiments – Methods and applications Optimization techniques: Concept of optimization, optimization parameters, classical optimization. Statistical design (Simplex and factorial design)

4. STABILITY TESTING - DRUGS AND DOSAGE FORMS **04Hrs.**

(Marks allotment : 10)

Solid state drug stability, dosage form stability, accelerated stability testing, shelf life calculations, strategies for prolonging shelf life. Effect of packaging materials on dosage form stability. Basic principles of ICH, stability testing of new drug substance and formulations, photostability testing and oxidative stability, role of containers in stability testing. WHO stability guidelines.

5. cGMP, ISO 9000 & 14000 SERIES, VALIDATION **06 Hrs.**

(Marks allotment : 20)

ISO 9000 & 14000 series, guide to Phamaceutical manufacturing facilities, cGMP considerations with emphasis on documentation practices.

Validation- General concepts, types, approaches to validation and scope of validation. Relationship between calibration, validation & qualification. Validation master plan, qualifications of utilities - HVAC systems, validation of water systems. Validation of manufacturing process for sterile and non-sterile products (briefly protocols and reports), Equipment qualification and cleaning validation.

6. INVENTORY MANAGEMENT **03 Hrs.**

(Marks allotment : 10)

Costs in inventory, inventory categories- special considerations, selective inventory control, reorder quantity methods and EOQ, inventory models, safety stock – stock out, lead time – reorder time methods, modern inventory management systems, inventory evaluation.

7. MATERIAL MANAGEMENT **06 Hrs.**

(Marks allotment : 15)

Materials–quality and quantity, value analysis, purchasing–centralized and decentralized, vendor development, buying techniques, purchasing cycle and procedures, stores management, salvaging and disposal of scrap and surplus. Selection of material handling systems, maintenance of material handling equipment, unit-load, pelletization and containerization, types of material handling systems.

8. PILOT PLANT SCALE UP TECHNIQUES **06 Hrs.**

(Marks allotment : 15)

Scale up of batches for product development, layout of pharmaceutical pilot plant, organization structure, personnel, activities. Pilot plant of tablets, capsules, solutions, dispersions, semisolids, and parenterals. Protocols for technology transfer. Process automation technology (PAT) in Pharmaceutical manufacturing. Introduction to SUPAC guidelines.

9. IPR AND REGULATORY GUIDELINES **07 Hrs.**

(Marks allotment : 15)

Definition, Need for patenting, Types of Patents, Conditions to be satisfied by an invention to be patentable, Introduction to patent search. Parts of patents. Filling of patents. The essential elements of patent; Guidelines for preparation of laboratory note book, Non-obviousness in Patent. Brief introduction to Trademark protection and WHO Patents. IPR's and its types, Major bodies regulating Indian Pharmaceutical sector, CDSCO. WHO, USFDA, EMEA, TGA, MHRA, MCC, ANVISA regulatory requirements for contract research organization. Regulations for Biosimilars. Role of GATT, TRIPS, and WIPO.

10. INDUSTRIAL HAZARDS AND PLANT SAFETY **03 Hrs.**

(Marks allotment : 5)

Industrial accidents, mechanical hazards, electrical hazards, chemical hazards, gas hazards, dust explosion, fire and explosion hazards, prevention and control of all these hazards, safety management. Industrial pollution and Control measurements.

PRACTICALS (T:6Hours/Week)

1. Preformulation study of tablet formulation using various diluents
2. Preformulation study of tablet formulation using various binders.
3. To study the effect of surfactants/Co-solvents on the solubility of drugs.
4. To study the effect of various excipients on the compressibility of tablets.
5. Preparation and evaluation of Diclofenac sodium gel containing different gel bases.
6. Study of the effects of pH on rheological characteristics of carbopol gels using Brookefield viscometer.
7. cGMP considerations for tablets.
8. cGMP considerations for injectables.
9. Preparation and comparative evaluation with marketed product for efficiency of neutralizing property of antacid suspensions.
10. Process validation of tablets.
11. Equipment qualification of an analytical instrument.
12. Equipment qualification of processing equipment.
13. Cleaning validation of an equipment.
14. Designing of plant layouts for tablets and parenterals.
15. Stability studies of dosage form at 30°C±2, 65±5 %RH and 40°C±2, 75±5% RH.

SCHEME OF EXAMINATION

1. Synopsis - 20 marks

2. Experiment

Major - 35 marks

Minor - 25 marks

3. Viva-voce - 20 marks

Total - 100 marks

REFERENCE BOOKS

1. Theory and Practice of Industrial Pharmacy By Lachmann and Libermann , Latest edition.
2. Modern Pharmaceutics by Gillbert and S. Banker 4th Edition .
3. Pharmaceutical Process Validation: By Fra R. Berry and Robert A. Nash, Vol 57, 2nd edition
4. Applied Production and Operation Management By Evans, Anderson and Williams GMP for pharmaceuticals Material Management by K.K. Ahuja Published by CBS publishers
5. Pharmaceutical Preformulations by J.J Wells
6. Pharmaceutical Dosage Forms: Tablets vol 1-3 by Leon Lachmann
7. Text book of Remington's Pharmaceutical sciences Vol I and II, 21st edition
8. Physical Pharmaceutics by Alfred Martin, 4th edition
9. Bentley's textbook of Pharmaceutics-Rawbins
10. ISO 9000-Norms and explanations
11. GMP for pharmaceuticals- Willing S.H. Marcel and Dekker
12. Pharmaceutical powder compaction technology by Goran Alderborn, 1996. Marcel and Dekker
13. D and C act by Vijay Malik, Latest edition, Eastern book company, Lucknow

JOURNALS

1. Drug Development and Industrial pharmacy
2. Indian Journal of Pharmaceutical sciences
3. Journal of Pharmaceutical Sciences
4. Indian drugs

URL's

1. www.cdsco.nic.in
2. www.journals.elsevier.com
3. www.fda.gov/
4. www.mhra.gov.uk
5. www.anvisa.gov.br/eng/legis/index.htm
6. www.pharmaguideline.com/2010/10/mcc.html
7. www.biosimilarnews.com/european-biosimilars-guidelines.