SYLLABUS FOR THE PRELIMINARY TEST FOR THE RECRUITMENT OF THE POST OF SENIOR SCIENTIFIC OFFICER, CLASS-1(DRUG)

TOTAL QUESTIONS: 200 TOTAL MARKS:200 MEDIUM: ENGLISH

1. MODERN PHARMACEUTICAL ANALYTICAL TECHNIQUES

1.1 UV-Visible spectroscopy: Basics of spectroscopy, Lambert-Beer's law and its deviation, nature of electronic excitations, origin of UV-Visible spectra, Chromophore, auxochrome, shifts in UV-Visible spectroscopy, Effect of Conjugation, Solvents and effects of solvent polarity, Instrumentation, Interpretation of UV spectra, Analytical method development for multicomponent formulations.

1.2 IR spectroscopy: Theory-Infrared absorption process, Modes of molecular vibrations, Factors affecting vibrational frequencies, Instrumentation: Dispersive, Fourier-Transform and ATR IR spectrometer, Sample handling, Applications of IR spectroscopy and Interpretation of IR spectra of organic compounds.

1.3 Spectroflourimetry: Theory of fluorescence and phosphorescence, Factors affecting fluorescence, Quenchers, Instrumentation, Applications of fluorescence spectroscopy.

1.4 Flame emission and Atomic absorption spectroscopy: Principle, Instrumentation, Interferences and Applications.

1.5 NMR spectroscopy: Nuclear spin states, Nuclear magnetic moments, Chemical and magnetic equivalence, Chemical shift and factors influencing chemical shift, Spin-Spin coupling, coupling constant and factors affecting coupling constant, Nuclear magnetic double resonance, NMR solvents, and shift reagents, Nuclear magnetic resonance spectrometer: Continuous-Wave and Pulsed Fourier Transform, Interpretation of organic compounds.

^{13}C NMR spectroscopy: Chemical shift, Information from ^{13}C NMR, Spin-spin splitting in ^{13}C NMR, Nuclear Overhauser Effect and Distortion less enhancement by polarization transfer (DEPT).

Difference between 1-D and 2-D NMR, NOESY and COSY, HETCOR, INADEQUATE techniques. Applications of 1D and 2D NMR spectroscopy.

1.6 Mass spectrometry: Principle, Ionization methods: Electron ionization, Chemical ionization, Desorption ionization techniques and Electrospray Ionization, Mass analyzers: Magnetic sector, Double-focusing, Quadrupole Time-of-Flight, Detection and Quantitation: Mass Spectrum, Determination of molecular weight and molecular Formulas, molecular ion peaks, isotopic peaks, metastable ion peaks and their role in

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determination of molecular weight, Fragmentation rules and processes: Radical-Site Initiated Cleavage: α-Cleavage, Charge-Site Initiated Cleavage: Inductive Cleavage, Two-Bond Cleavage, Retro Diels-Alder Cleavage, McLafferty Rearrangements , Interpretation of Mass spectra, applications of Mass spectrometry.

1.7 Chromatography

1.7.1 Basics of chromatography-Fundamentals of chromatography: Principles and modes of chromatographic separations, chromatographic behaviour of solutes: Retention, Partition coefficient, Partition ratio, relative retention, Column efficiency and resolution: Plate height and plate number, Band asymmetry, Resolution; Column processes and Band broadening: van Deemter equation; Peak area integration.

1.7.2 Principle, apparatus/instrumentation and applications of Paper chromatography, Thin Layer chromatography, High Performance Thin Layer chromatography, Column chromatography, High Performance Liquid chromatography, Gas chromatography, Ion exchange chromatography, Size Exclusion and Affinity chromatography, Hyphenated techniques: GC-MS, LC-MS, analytical method development by chromatographic methods.

1.7.3 Electrophoresis: Principle, Electrophoretic mobility and factors affecting it, Instrumentation and applications of Paper electrophoresis, Gel electrophoresis, Capillary electrophoresis, Zone electrophoresis, Moving boundary electrophoresis, Iso electric focusing.

1.8 Thermal methods of analysis: Introduction, Principle, Instrumentation and Applications of Differential scanning calorimetry, Differential thermal analysis and Thermogravimetric analysis.

1.09 Immunoassays: Basic principle, Types of immunoassay: Enzyme immunoassay or Enzyme-linked immunosorbent assay, Radioimmunoassay, Fluoroimmnoassay, Chemiluminescence immunoassay, Quantification and applications of Immunoassays.

1.10 Bioassay: Principle, types and applications.

2. IMPURITY PROFILING AND STABILITY STUDIES

2.1 Impurity profiling: Definition, classification of impurities in drug substance or Active Pharmaceutical Ingredients, quantification of impurities as per ICH guidelines and qualification of impurities, Analytical procedures.

Impurities in new drug products: Rationale for the reporting and control of impurities, listing of impurities in specifications,

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Residual solvents as impurities: General principles, classification of residual solvents, Analytical procedures, limits of residual solvents, reporting levels of residual solvents.

2.2 Elemental impurities: Element classification, control of elemental impurities, Potential Sources of elemental Impurities, Identification of Potential Elemental Impurities, analytical procedures.

2.3 Stability testing of Pharmaceuticals: Concept of stability, stability testing & shelf life calculation, WHO and ICH stability testing guidelines, Stability zones, steps in development, practical considerations.

Stability testing protocols: Selection of batches, container closure system, test parameters, sampling frequency, specification, storage conditions, recording of results.

Important mechanistic and stability related information provided by results of study of factors like temperature, pH, buffering species ionic strength and dielectric constant etc. on the reaction rates with practical considerations. Photostability testing guidelines. ICH stability testing guidelines.

2.4 Stability testing of phytopharmaceuticals: Regulatory requirements, protocols, HPTLC/HPLC, finger printing, interactions and complexity.

3. HERBAL AND COSMETIC ANALYSIS

3.1 Herbal drug standardization: WHO and AYUSH guidelines.

3.2 Adulteration and Deterioration: Introduction, types of adulteration/substitution of herbal drugs, Causes and Measure of adulteration, Sampling Procedures, Determination of Foreign Matter, heavy metals, pesticide residues, phototoxin and microbial contamination in herbal formulations. Finger printing techniques in identification of drugs of natural origin.

3.3 Regulatory requirements for setting herbal drug industry: Global marketing management, Indian and International patent law as applicable to herbal drugs and natural products and its protocol.

3.4 Testing of natural products and drugs: Adulterant Screening using modern analytical instruments, Regulation and dispensing of herbal drugs, Stability testing of natural products, protocol.

Monographs of Herbal drugs: Study of monographs of herbal drugs and comparative study in IP, USP, Ayurvedic Pharmacopoeia, American herbal Pharmacopoeia, British Herbal Pharmacopoeia, Siddha and Unani Pharmacopoeia, WHO guidelines in quality assessment of herbal drugs.

3.5 Structural characterization of natural compounds using IR, ^{1}HNMR, ^{13}CNMR spectroscopy and Mass spectrometry.

3.6 Evaluation of cosmetic products: Determination of acid value, ester value, saponification value, iodine value, peroxide value, rancidity, moisture content, ash value, volatile matter, heavy metals, fineness of powder, density, viscosity of cosmetic raw materials and finished products. Study of quality of raw materials and general methods of analysis of raw material used in cosmetic manufacture as per Bureau of Indian Standards.

Indian Standard specification laid down for sampling and testing of various cosmetics in finished forms such as baby care products, skin care products, dental products, personal hygiene preparations, lips sticks. Hair products and skin creams by the Bureau of Indian Standards.

4. QUALITY CONTROL AND QUALITY ASSURANCE

4.1 Introduction: Concept, evolution and scopes of Quality Control, Quality Assurance, Quality Audit and GMP.

4.2 Organization and personnel: Personnel responsibilities, training, hygiene and personal records.

Premises: drug industry location, Design, construction and plant layout, maintenance, sanitation, environmental control, utilities and maintenance of sterile areas, control of contamination.

Equipment's and raw materials: Equipment selection, purchase specifications, maintenance, purchase specifications and maintenance of stores for raw materials.

4.3 Manufacturing operations and controls: Sanitation of manufacturing premises, mix-ups and cross contamination, processing of intermediates and bulk products, packaging 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. Complaints and evaluation of complaints.

4.4 Analysis of raw materials, finished products, packaging materials, in process quality control (IPQC), Developing specification (ICH Q6 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,

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creams, parenterals, ophthalmic and surgical products. Quality control test for containers, rubber closures and secondary packing.

4.5 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.

4.6 Calibration and Validation: Introduction, definition and general principles of calibration, qualification and validation, importance and scope of 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.

5. QUALITY MANAGEMENT SYSTEMS

5.1 Introduction to Quality: Evolution of Quality, Definition of Quality, Dimensions of 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 behaviour, concept of internal and external customers. Case studies. Cost of Quality: Cost of quality, Categories of cost of Quality, Models of cost of quality, optimising costs, Preventing cost of quality.

5.2 Pharmaceutical quality Management: Basics of Quality Management, Total Quality Management (TQM), Principles of Six sigma, 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. Pharmaceutical Quality Management – ICH Q10,

Knowledge management, Quality Metrics, Operational Excellence and Quality Management Review. Quality Audit.

5.3 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.

5.4 Six System Inspection model: Quality Management system, Production system, Facility and Equipment system, Laboratory control system, Materials system, Packaging and labelling system. Concept of self-inspection.

5.5 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, Annual Product Reviews, Batch Review and Batch Release, area clearance/ Line clearance.

5.6 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.

6. PHARMACEUTICAL REGULATORY AFFAIRS

6.1 Good Regulatory Practices: Introduction: CDSCO, USFDA (inclusive of CDER and CBER), EMEA, WHO and Pharmaceutical Inspection Convention (PIC). Regulatory Concepts Basic terminology, guidance, guidelines, regulations, Laws and Acts, Orange book, Federal Register, Code of Federal Regulatory, Purple book.

6.2 Current Good Manufacturing Practices: Introduction, cGMP guidelines according to schedule M, Sch M III and other relevant CDSCO regulatory guidance documents. US cGMP Part 210 and Part 211., CFR-21 part 11. 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. OSHAS guidelines, Good Warehousing Practice.

6.3 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, NABL certification and accreditation,

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protocol for conduct of non-clinical testing, control on animal house, report preparation and documentation. CPCSEA guidelines.

6.4 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.

6.5 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.

6.6 The International Conference on Harmonization (ICH) process, ICH guidelines to establish quality, safety and efficacy of drug substances and products, Overview of ICH Guidelines-QSEM, with special emphasis on Q-series guidelines. ISO 9000 & ISO14000: Overview, Benefits, Elements, steps for registration, ISO 9001:2008, 9001:2015, ISO 14001:2004. Introduction, scope and importance of intellectual property rights. Concept of trade mark, copyright and patents.

7. PHARMACEUTICAL JURISPRUDENCE

Drugs and Cosmetics Act, 1940 and its rules 1945, Pharmacy Act-1948, Narcotic Drugs and Psychotropic substances Act-1985 and Rules, Drugs and Magic Remedies Act and its rules, Prevention of Cruelty to animals Act-1960, National Pharmaceutical Pricing Authority, Code of Pharmaceutical ethics, Right to Information Act, 2005.

8. HUMAN ANATOMY AND PHYSIOLOGY

Introduction to human body, Cellular level of organization, Tissue level of organization, Integumentary system, Skeletal system, Joints, Body fluids and blood, Lymphatic system, Peripheral nervous system, Special senses, Cardiovascular system, Nervous system, Digestive system, Energetics, Respiratory system, Urinary system, Endocrine system, Reproductive system, Introduction to genetics.

9. PATHOPHYSIOLOGY

Basic principles of Cell injury and Adaptation, Basic mechanism involved in the process of inflammation and repair, Cardiovascular System, Respiratory system, Renal system, Haematological Diseases, Endocrine system, Nervous system, Gastrointestinal

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system, Inflammatory bowel diseases, jaundice, hepatitis (A,B,C,D,E,F), alcoholic liver disease, Disease of bones and joints, Principles of cancer, Infectious diseases, Sexually transmitted diseases.

10. PHARMACOLOGY AND PHARMACOLOGICAL SCREENING

10.1 General Pharmacology: Pharmacokinetics; dynamics of drug absorption, distribution, biotransformation and elimination, Significance of Protein binding, Pharmacodynamics; Mechanism of drug action and the relationship between drug concentration and effect. Receptors, structural and functional families of receptors, quantitation of drug receptors interaction and elicited effects.

10.2 Neurotransmission: General aspects and steps involved in neurotransmission, Neurohumoral transmission in autonomic nervous system: Adrenaline and Acetyl Choline, Neurohumoral transmission in central nervous system: histamine, serotonin, dopamine, GABA, glutamate and glycine, Non-adrenergic non-cholinergic transmission, Co-transmission.

10.3 Common laboratory animals: Description, handling and applications of different species and strains of animals. Transgenic animals: Production, maintenance and applications Anaesthesia and euthanasia of experimental animals. Maintenance and breeding of laboratory animals. CPCSEA guidelines to conduct experiments on animals.

10.4 Preclinical screening of new substances for the pharmacological activity using in vivo, in vitro, and other possible animal alternative models for

- Behavioural and muscle co-ordination, CNS stimulants and depressants, anxiolytics, anti-psychotics, anti-epileptics, Drugs for neurodegenerative diseases like Parkinsonism, Alzheimers.
- Drugs for metabolic disorders like anti-diabetic, anti-dyslipidemic agents.
- Cardiovascular Pharmacology: Antihypertensives, antiarrhythmics, antianginal, antiatherosclerosis agents and diuretics.
- Anti-cancer agents and Hepatoprotective screening methods.
- Analgesics, anti-inflammatory, antipyretic agents. Gastrointestinal drugs: anti-ulcer, anti -emetic, anti- diarrheal and laxatives.

11. PHARMACEUTICS

11.1 Classification and definitions of different dosage forms

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11.2 Introduction to pre-formulation and study of physical and chemical characteristics of drug substances. Application of pre-formulation considerations in the development of solid, liquid oral and parenteral dosage forms.

11.3 Properties and applications of different types of formulation additives, e.g., diluents, binders, disintegrating agents, lubricants, glidants, vehicles, antioxidants, preservatives, colouring, flavouring, sweetening, suspending, emulsifying agents, solubilizers, Mixed solvency concept (solubilizers), hydrotropic agents, materials for ointments and suppository bases.

11.4 Study of following dosage forms: Solution, Suspension, Emulsion, Tablet, Capsule, Parenterals and Ophthalmic preparations.

11.5 Basic concepts, advantages/disadvantages, factors influencing, physicochemical & biological approaches for Sustained/Controlled release formulation, Mechanism of Drug Delivery from SR/CR formulation.

12. PHARMACEUTICAL CHEMISTRY

12.1 Organic intermediates: Carbocations, carbanions, free radicals, carbenes and nitrenes. Their method of formation, stability and synthetic applications. Types of reaction mechanisms and methods of determining them.

12.2 Types of reactions, mechanisms and their relative reactivity and orientations: Substitution, Addition, Nucleophilic, Elimination and Rearrangement reactions and factors affecting a reaction.

12.3 Role of protection of different functional groups in organic synthesis, b. Protection for the hydroxyl group, including 1,2-and1,3-diols: ethers, esters, carbonates, cyclic acetals & ketals, c. Protection for the Carbonyl Group: Acetals and Ketals, d. Protection for the Carboxyl Group: amides and hydrazides, esters, e. Protection for the Amino Group and Amino acids: carbamates and amides.

12.4 Organic Name reactions with their respective mechanism and application involved in synthesis of drugs containing five, six membered and fused heterocycles such as Debus-Radziszewski imidazole synthesis, Knorr Pyrazole Synthesis, Pinner Pyrimidine Synthesis, Combes Quinoline Synthesis, Bernthsen Acridine Synthesis, Smiles rearrangement and Traube purine synthesis.

12.5 Synthon approach and retrosynthesis applications:

a. Basic principles, terminologies and advantages of retrosynthesis; guidelines for dissection of molecules. Functional group inter-conversion and addition (FGI and FGA)

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b. C-X disconnections; C-C disconnections- alcohols and carbonyl compounds; 1,2-, 1,3-,1,4-, 1,5-, 1,6-difunctionalized compounds c. Strategies for synthesis of three, four, five and six-membered ring.

13. MEDICINAL CHEMISTRY

13.1 Physicochemical properties in relation to biological action; Ionization, Solubility, Partition Coefficient, Hydrogen bonding, Protein binding, Chelation, Bio-isosterism, Optical and Geometrical isomerism.

13.2 Drug metabolism principles-Phase I and Phase II, Factors affecting drug metabolism including stereo chemical aspects.

13.3 Drug discovery: Stages of drug discovery, lead discovery; identification, validation and diversity of drug targets.

13.4 Biological drug targets: Receptors; types, binding and activation, theories of drug receptor interaction, drug receptor interactions, agonists vs antagonists. Enzymes: Reversible and Irreversible inhibitors, Inhibitors acting at allosteric binding sites, Uncompetitive and non-competitive inhibitors, Transition-state analogues, Suicide substrates, Isozyme selectivity of inhibitors and Medicinal uses of enzyme inhibitors.

13.5 Prodrug Design: Basic concept, Carrier linked prodrugs, functional groups, Prodrugs to improve patient acceptability, Drug solubility, Drug absorption and distribution, site specific drug delivery and sustained drug action. Rationale of prodrug design and practical consideration of prodrug design.

14. PHARMACOGNOSY

14.1 Introduction to Pharmacognosy and Classification of drugs of natural Origin.

14.2 Morphological and microscopical examination of drugs, Cell differentiation and ergastic cell contents and Techniques in microscopy.

14.3 General Methods for extraction, isolation and identification of Volatile oils, Alkaloids, Flavonoids, Glycosides and Tannins.

14.4 Methods of preparation of Arista, Asava, Lehya and Bhasma.

14.5 Source, chemical constituents, uses, and adulteration of the following natural drugs: Rauwolfia, Ipecacuanha, Belladonna, Cinchona, Senna, Aloe, Noxvomica, Cinnamon, Digitalis, Opium, Kurchi, Brahmi, Tulsi, Bael and Ephedra

15. Current trends and recent advancement in the Pharmaceutical Sciences.

16. Use of Artificial Intelligence in drug discovery.

(NASIM MODAN)
DEPUTY SECRETARY
GUJARAT PUBLIC SERVICE COMMISSION

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