

# SYLLABUS FOR PHARMACEUTICAL MEDICINE

September 2008

## INTRODUCTION

The content of the Syllabus is listed under the separate Sections below. There is a considerable degree of overlap; some topics appear in more than one Section and it is not intended to imply that any topic is restricted only to those Sections under which it is listed. The order of listing does not reflect importance.

The Syllabus for Pharmaceutical Medicine is composed of eight Sections:

1. Medicines Regulation
2. Clinical Pharmacology
3. Statistics and Data Management
4. Clinical Development
5. Healthcare Marketplace
6. Drug Safety and Pharmacovigilance
7. Discovery of New Medicines
8. Therapeutics

## SECTION 1. MEDICINES REGULATION

- The general principles of medicines regulation
- Medicines regulation in UK, EU, USA, Japan
- Activities and contribution of International Conference on Harmonisation
- Good Manufacturing Practices, Good Laboratory Practices, Good Clinical Practices
- Clinical Trials regulations - IND, CTA, EU Directives etc
- Common Technical Document, Overviews
- Key pharmacovigilance regulations including reporting of adverse drug reactions, Periodic Safety Update Reports
- Product information - Summary of Product Characteristics, Prescribing Information/Package Insert, Patient Information Leaflets
- Licensing - MAA, NDA, abridged applications, updating and maintaining licences
- Orphan drugs
- Provisions for and use of unlicensed medicines
- Drug abuse and dependence
- Non-prescription drugs and reclassification of Prescription Only and Pharmacy only medicines

- Medical device regulations
- Fraud and professional misconduct
- Product defects and recall
- Ethics and Ethics Committees
- Pharmacopoeias

## **SECTION 2. CLINICAL PHARMACOLOGY**

### ***NON -CLINICAL DEVELOPMENT TO SUPPORT TESTING IN HUMANS***

- Safety testing - acute, subacute toxicology, genotoxicology, reproductive toxicology, local tolerance, safety pharmacology, hypersensitivity and immunotoxicology, carcinogenicity
- Small molecules and biologicals
- Pharmacokinetics; *in vitro* and *in vivo* study of metabolism; ADME
- Pharmaceutical development of drug substance and drug product: formulations, manufacture and supply of materials, labelling and presentation, stability and storage, purity, compatibility, disposal

### ***EXPLORATORY CLINICAL DEVELOPMENT***

- Assessment of non-clinical data
- Planning of studies in Exploratory Development
- Populations for exploratory studies - healthy volunteers and patients
- Dose selection
- Ethics - principles, peer review, informed consent, Declaration of Helsinki, protection of research subjects, minimising risk
- Regulation
- Studies - objectives, design, conduct and analysis, choice of site
- Tolerability and safety
- Use of biomarkers and pharmacodynamic endpoints, imaging, dose-response, proof-of-concept, disease models
- Pharmacokinetics, ADME and pharmacokinetic/pharmacodynamic models
- Interpretation of study design, analysis and results

### ***CLINICAL PHARMACOKINETICS***

- Concepts - half-life, volume of distribution, clearance
- Bioavailability and bioequivalence
- Drug-drug and drug-disease interactions (extrinsic factors)
- Studies in different populations (intrinsic factors)

- Pharmacogenetics
- Population pharmacokinetics
- Applicability of pharmacokinetics to dosage regimen and study design

## **SECTION 3. STATISTICS AND DATA MANAGEMENT**

### ***THE PURPOSE AND FUNDAMENTALS OF STATISTICS***

#### ***TRIAL DESIGN, HYPOTHESIS TESTING, POWER***

- Pre-trial decisions and specification
- Risk factors, confounding variables
- The null hypothesis, Type I and II errors, significance, power
- Minimising bias

#### ***MEASUREMENT AND TYPES OF DATA***

- Standardisation
- Variations in biometry in population, in disease
- Patient instruments

#### ***DATA COLLECTION AND MANAGEMENT***

- Options for data collection (manual and electronic)
- Creation, maintenance and security of databases, software validation and archiving
- Data management from clinical trials: source documents, corrections, computer capture, verifications and extraction, coding
- Within-trial decisions, data management, extraction and manipulation

#### ***TYPES OF ANALYSIS***

- Analysis of efficacy end-points and of safety
- Interim analysis
- Paired and non-paired tests, parametric and non-parametric tests, confidence limits
- Handling of rating and visual analogue scales, patient diaries and laboratory values
- Sensitivity and specificity of indices
- True and apparent incidence and prevalence data

### ***INTERPRETATION OF STUDY DESIGN, ANALYSIS AND RESULTS***

- Assessment of violations, withdrawals, errors, bias
- Statistical principles and issues in report writing: data manipulation, transposition, merging
- Clinical interpretation of trial results
- Final report writing and formatting for registration dossier and publications

## **SECTION 4. CLINICAL DEVELOPMENT**

### ***PLANNING AND ORGANISATION***

- Organisation and operation of project teams
- Target product profile, target label, clinical development plans
- Integrated project planning
- Expanded access programmes
- Paediatric programme planning
- Requirements for licensing of new medicines
- Budgeting and costs control

### ***REGULATION AND ETHICS***

- In UK, EU, USA, Japan to include:
  - EU Directives and Guidances
  - ICH - Good Clinical Practices
  - Ethics - principles, peer review, Declaration of Helsinki, informed consent
  - Regulatory review
  - Indemnity and compensation
  - Confidentiality and data protection

### ***INTERVENTIONAL AND NON-INTERVENTIONAL CLINICAL TRIALS***

- Planning of pre-licensing and post-licensing clinical trial programmes - use of non-clinical and existing clinical trial data
- Study types and designs; choice of comparator
- Documentation – writing and reviewing protocol and reports, source document review, case report form design and review, study master file preparation
- Investigator's brochure content, review and maintenance
- Contractual arrangements with investigators and contract research organisations
- Study conduct
- Quality control and quality assurance

- Adverse Events and Serious Adverse Events - definitions, collection, reporting, reconciliation, assessment and coding review
- Aggregate clinical trial report reviews, including annual reports and common technical document summaries
- Interpretation of study design, analysis and results
- Formulations, manufacture and supply of materials, labelling and presentation, stability and storage, purity, compatibility, disposal
- Data management and statistical analysis

## **SECTION 5. HEALTHCARE MARKETPLACE**

- Quality of Life
- Intellectual property, legal issues, parallel imports
- Marketing structure and competition, price negotiations
- National and local formularies
- Product information, advertising and claims
- Product support and promotion
- Product life-cycle management
- Product liability and compensation
- Legal and regulatory framework and industry self-regulation; codes of practice covering advertising including those of the MHRA (Advertising and Promotion of Medicines in the UK, the Blue Guide), ABPI and EFPIA
- Principles and practice of marketing
- Measurement of healthcare, governmental policy and third-party reimbursement
- Principles of health economics
- Pharmacoepidemiology
- Competition, in-licensing, co-marketing

## **SECTION 6. DRUG SAFETY AND PHARMACOVIGILANCE**

### ***PHARMACOVIGILANCE***

- The role of the pharmaceutical physician in pharmacovigilance and drug safety
- Periodic Safety Update Reports
- Main sources of epidemiological pharmacovigilance information
- Signal detection, interpretation and management
- Post-authorisation safety studies
- Benefit-risk assessment
- Issue and crisis management

### **ADVERSE EVENTS AND ADVERSE DRUG REACTIONS**

- Mechanisms and classification of Adverse Events and Adverse Reactions
- Collection of AEs in Clinical Trials
- Spontaneous reporting post-marketing
- Role of sponsors and investigators in reporting and regulatory requirements (EMA Guidance)
- Predisposing factors in health and disease
- Dosage, accumulation, medication errors and interactions
- Assessment of evidence for causality and association
- Product labelling including Summary of Product Characteristics/Prescribing Information/Package Insert and Patient Information Leaflets

### **MANAGING RISK**

- Risk management
- Safety specification
- Dear Healthcare Professional Communication
- Product withdrawal procedures
- Drug abuse and dependence
- Off label use and misuse

## **SECTION 7. DISCOVERY OF NEW MEDICINES**

- The philosophy behind and organisation of research
- Disease target identification and selection
- Patenting new active substances
- Natural products; novel indications
- Receptor-based approaches, agonists, antagonists, enzyme inhibitors, genomics, proteomics
- Lead optimisation and candidate selection of molecules for exploratory human investigation
- *In vitro* and *in vivo* testing of new compounds
- Relationship between animal and human pharmacology

## **SECTION 8. THERAPEUTICS**

- Major drug classes (including biologicals): mode of action, use, safety
- Measurement of drug effects

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- Adverse drug reactions
- Benefit:risk
- Drug interactions
- Prescribing for particular populations e.g. children, elderly, pregnant and breast feeding women, patients with renal or hepatic impairment
- Controlled drugs and drug dependence
- Overdosage and treatment of poisoning
- Patient compliance and information
- Therapeutic drug monitoring

*(End)*