PHARMATRAIN SYLLABUS 2010

SYLLABUS FOR PHARMACEUTICAL MEDICINE / DRUG DEVELOPMENT SCIENCE

SECTION 1. Discovery of Medicines		
1.1	Strategy and organisation of research including collaborative approaches e.g. with academia	
1.2	Disease models, target identification, validation and selection	
1.3	Receptor-based approaches: agonists, antagonists, enzyme inhibitors, genomics, proteomics	
1.4	The principle steps in discovering, modifying, assessing and patenting new chemical and biological compounds	
1.5	Other therapeutic approaches e.g. advanced therapies, phytotherapies, herbal products	
1.6	Lead optimisation and candidate compound selection for further development	
1.7	*In vitro* and *in vivo* testing of new compounds	

1.8	Principles of translational medicine	
1.9	Relationship between animal and human pharmacology and physiology e.g. biomarkers, modeling and simulation	
SECTION 2. Development of Medicines: Planning		
2.1	The elements and functions necessary in the integrated development of a new medicine at a corporate and international level	
2.2	Quality management	
2.3	Project management techniques: drug development plan project teams, tools and decision-making from target product profile (TPP) and target product claims (TPC) to registration dossier submission	
2.4	Programme planning in special cases e.g. paediatrics, orphan drugs, elderly	
2.5	Programmes in developing countries	
2.6	R&D portfolio planning including in- and out-licensing of new medicines	
2.7	Resource planning: budgeting and cost control	
SECTION 3. Non-Clinical Testing		
3.1	Pathophysiology-based pharmacology	
3.2	Differences in non-clinical safety and toxicity packages between small molecules and biologicals	
3.3	The fundamental differences and similarities between the pharmacology and toxicology of compounds and their metabolites in animals and man, and their qualitative and quantitative assessment	
3.4	The purpose of descriptive and quantitative *in vitro* and *in vivo* testing	
3.5	The choice of and the predictive value of these tests for acute, chronic, reproductive, genetic and immune toxicology, and carcinogenicity	
3.6	Common mechanisms of damage to organs and their detection or elucidation	
3.7	The scheduling of toxicology tests linked to development plans, to regulatory needs, to human and animal pharmacology, and to intended clinical use and route(s) of administration	
3.8	The size, cost and administration of the toxicology programme; its data management, quality assurance and report writing	
3.9	The regular review of toxicology, its inclusion into clinical trial protocols, and investigator brochures, and the appropriate planning and correlation with the clinical evaluation of potential and observed toxicity in patients	
3.10	Safety pharmacology, hypersensitivity	
3.11	Toxicokinetics; *in vitro* and *in vivo* study of metabolism; ADME	

SECTION 4. Pharmaceutical Development		
4.1	Pharmaceutical development of drug substance and drug product: formulations, manufacture and supply of materials, labelling and presentation, stability and storage, purity, compatibility, disposal including biotechnology products	
4.2	The economic primary production of new compounds and secondary production of research and market formulations	
4.3	The choice of formulations depending upon the characteristics of the compound and the intended uses of the product	
4.4	The principles of testing formulations for bioequivalence, stability, impurity and incompatibility leading to a final specification, including the development of biosimilar formulations	
4.5	The concept of blinding: preparing matching placebo and competitor products	
4.6	Planning clinical trials supply requirements; packaging and labelling of clinical trial supplies (including stability and storage requirements); distributing supplies and disposing of remaining stocks	
SECTION 5. Exploratory Development (Molecule to Proof-of-Concept)		
5.1	Intended therapeutic indications, biomarkers, efficacy end-points and criteria for 'go, 'no-go' decisions	
5.2	Assessment of non-clinical data and risk as prerequisite before administration to man	
5.3	Exploratory phase 0 trials	
5.4	The early clinical development plan: the objectives, design, conduct and analysis of early exploratory development studies: modelling and simulation, tolerability, metabolism, pharmacokinetics, pharmacodynamics and safety in man, problems of participant's safety in the concept of blinding.	
5.5	Pharmacokinetics, ADME and pharmacokinetic / pharmacodynamic models	
5.6	Concepts of half-life, volume of distribution, clearance	
5.7	Bioavailability and bioequivalence	
5.8	Drug-drug and drug-disease interactions (extrinsic factors)	
5.9	Studies in different populations (intrinsic factors)	
5.10	Population pharmacokinetics	
5.11	Pharmacogenetics / pharmacogenomics	
5.12	Applicability of pharmacokinetics to dosage regimen and study design	
5.13	First administration to patients: principles of proof of concept and dose-finding studies	
5.14	Impact of results on planned therapeutic indications, on predicted dosage schedule, on additionally required animal toxicology and on drug delivery concepts / forms	

SECTION 6. Confirmatory Development: Strategies (Proof-of-Concept to Market)		
6.1	Final definition of therapeutic indications, categories of patients, delivery system(s), dosage forms and dosage regimens	
6.2	Planning and global coordination / harmonisation of pre-licensing and post-licensing clinical trial programmes; use of non-clinical and existing clinical trial data	
6.3	Estimated treatment population, clinical trial supplies and costs up to registration	
6.4	Decision points, schedules and resources required for a confirmatory clinical development plan (CDP)	
6.5	Life-cycle management planning: extension of therapeutic claims, new formulations, new dosage schedules by peri-marketing trials, post-marketing (surveillance) studies and quality of life measures	
6.6	Regulatory review of existing and emerging research results	
6.7	Strategy for product life-cycle management	
SECTION 7. Clinical Trials		
7.1	Choice of trial design, of placebo and other comparators, of patient populations, of sample size, of locations, of randomisation, of end-points and of statistical analysis	
7.2	New trial designs e.g. adaptive design	
7.3	Non-interventional / observational study design	
7.4	Principles of Good Clinical Practice and procedures applied in all stages of the clinical trial process to ensure subject protection, scientific validity and safety	
7.5	Investigator's brochure: content, review and maintenance	
7.6	Protocol preparation according to ICH E6 and review	
7.7	Feasibility and investigator recruitment	
7.8	Pre-study visits and investigator meetings / investigator training	
7.9	Project management including resources / vendors and budget	
7.10	Contractual arrangements with investigators and contract research organisations including publication rights	
7.11	Clinical trial registries	
7.12	Investigative site management	
7.13	Study medication handling and drug accountability	
7.14	Adverse event assessment and reporting; emergency coverage	
7.15	Monitoring and source document verification	
7.16	Trial Master File	
7.17	Quality management system; SOPs; quality assurance and quality control;	

	independent audits; inspections,	
7.18	Aggregate clinical trial report reviews, including annual reports and common technical document summaries	
SECTION 8. Ethics and Legal Issues		
8.1	Ethical issues in biomedical research and pharmaceutical medicine.	
8.2	Ethics: principles, history incl. Declaration of Helsinki, Directive 2001/20/EC, ethical review, informed consent, safety and human dignity of research subjects.	
8.3	Protection of research subjects, minimising risk incl. site qualification assessment	
8.4	Ethical aspects in research questions and study designs for First-in-Human to post marketing and epidemiological studies, including placebo and comparator choice	
8.5	Conflict of interest and equipoise	
8.6	Ethical aspects in subject contact and recruitment	
8.7	Ethical issues in reimbursement, compensation and inducement	
8.8	Risks, benefits and burden of study participation	
8.9	The informed consent process	
8.10	Privacy, confidentiality and data protection	
8.11	Indemnity, insurance for participants/investigators/institutions, and complaint procedures	
8.12	Ethical aspects in study follow-on	
8.13	Ethical aspects in clinical trials in vulnerable populations	
8.14	Ethical aspects in advanced therapy medicinal products	
8.15	Ethical aspects in clinical trials in third world and emerging countries	
8.16	Fraud and misconduct in biomedical research and clinical development	
SECTION 9. Data Management and Statistics		
9.1	Options for data collection (manual and electronic) and standardisation	
9.2	Case report form (CRF) design and review	
9.3	Creation, maintenance and security of databases, software validation and archiving	
9.4	From source document to CRF completion, CRF review and corrections, data entry, query generation and resolution, coding of adverse events, database lock	
9.5	Within-trial decisions, data management, extraction and manipulation	
9.6	The purpose and fundamentals of statistics	
9.7	Role and responsibilities of the statistician	
9.8	The statistical analysis plan	
9.9	Trial design: pre-trial decisions and specifications; risk factors; confounding	

	variables	
9.10	Hypothesis testing: the null hypothesis, Type I and II errors, significance, power	
9.11	Sample size calculation	
9.12	Minimising bias	
9.13	Types of data and standardisation of measurement	
9.14	Patient-reported outcomes e.g. diaries, quality of life measures	
9.15	Statistical analysis of efficacy end-points and of safety	
9.16	Interim analysis	
9.17	Paired and non-paired tests, parametric and non-parametric tests, confidence limits	
9.18	Handling of rating and visual analogue scales, patient diaries and laboratory values	
9.19	Handling of missing data	
9.20	Sensitivity and specificity of tests	
9.21	True and apparent incidence and prevalence	
9.22	Interpretation of analyses; assessment of violations, withdrawals, errors, bias	
9.23	Statistical principles and issues in statistical report writing: data manipulation, transformation, merging, preparation of the statistical report	
9.24	Clinical interpretation of trial results	
9.25	Dealing with confounding factors and bias	
9.26	Critical review of publications.	
SECTION 10. Regulatory Affairs		
10.1	Background to and general principles of medicines regulation	
10.2	Philosophy of regulatory oversight; practical input of international bodies e.g. WHO, WMA, CIOMS etc and national agencies	
10.3	The evolution of control mechanisms; differences between agencies	
10.4	Activities and contribution of International Conference on Harmonisation (ICH).	
10.5	Good Manufacturing Practices; Good Laboratory Practices; Good Clinical Practices	
10.6	Integration of regulatory affairs into pre- and post-marketing; planning and review of product strategy.	
10.7	The approval, appeals and referrals processes in Europe, aspects of confidentiality / transparency and updating; maintaining Marketing Authorisations	
10.8	Orphan drugs, paediatric data, advanced therapies, biosimilars, generics	
10.9	Medicines regulation in EU in comparison with the USA, Japan and emerging markets	
10.10	Clinical Trials regulations; EU Directives and Guidances and their diversity in national implementation, CTA including IMPD substantial amendments. Clinical trial regulations in other regions e.g. the US IND process	

10.11	Common Technical Document (CTD and eCTD), Overviews	
10.12	The preparation and submission of marketing applications in major countries (MAA, NDA, JNDA, CNDA); regulatory management systems in Europe, US, Japan and local special regulatory requirements and the various authorisation procedures	
10.13	Product Information regulation: Summary of Product Characteristics; Package Insert; Patient Information Leaflets; Prescribing Information	
10.14	Advertising and promotion regulation: promotional material	
10.15	Prescription-only versus over-the-counter medicines	
10.16	Provisions for and use of unlicensed medicines.	
10.17	Product defects and recall	
10.18	Medical device regulations	
10.19	Pharmacopoeias	
10.20	Risk management: Risk Management Plans (RMPs) in the EU; Risk Evaluation and Mitigation Strategies (REMS) in the USA	
10.21	Safety Specification	
10.22	Direct Healthcare Professional Communication	
10.23	Product withdrawal procedures	
10.24	Drug abuse and dependence	
10.25	Off-label use and misuse	

SECTION 11. Drug Safety and Pharmacovigilance

11.1	The role of the pharmaceutical professional in drug safety and pharmacovigilance	
11.2	Assessment and classification of adverse events (AEs), adverse drug reactions (ADRs), Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reactions (SUSARs)	
11.3	The concept of benefit / risk assessment, determination of causal relationship between the medicinal product and the adverse event.	
11.4	Collection of adverse events in clinical trials	
11.5	Role of sponsors and investigators in reporting, and regulatory requirements	
11.6	Predisposing factors in health and disease	
11.7	Spontaneous reporting post-marketing	
11.8	Dosage, accumulation, medication errors and interactions	
11.9	Periodic Safety Update Reports	
11.10	Pharmacoepidemiology	
11.11	Main sources of epidemiological pharmacovigilance information	
11.12	Signal detection, interpretation and management	
11.13	Post-authorisation safety studies	

11.14	Post-authorisation risk management including Issue and crisis management	
11.15	Assessment of evidence for causality and association	
SECTION 12. Information, Promotion and Education		
12.1	Principles and practice of marketing, market analysis	
12.2	Information to patients and patient organisations, prescribing and compliance	
12.3	Product Information content and preparation: Summary of Product Characteristics; Package Insert; Patient Information Leaflets; Prescribing Information	
12.4	Product support and promotion	
12.5	Codes of conduct: promotional policy and procedures, Good Promotional Practice	
12.6	Advertising: claims, ethics, control and approval	
12.7	Publication strategy	
12.8	Sales representative training: material and aids	
12.9	Educational meetings; sponsored meetings and sponsored publications	
SECTION 13. Economics of Healthcare		
13.1	Principles of healthcare economics; principles of justice and equity in healthcare economics	
13.2	Evidence Based Medicine; outcomes research	
13.3	Quality of Life, concept and measurement instruments	
13.4	Market structure and competition, price negotiations, national and local formularies (reimbursement)	
13.5	Measurement of healthcare efficiency, governmental policy and third party reimbursement	
13.6	Economics of industry, competition, licensing, co-marketing	
13.7	Financial control, return on investment, fixed assets, budgeting, accounting, profitability	
13.8	Generics, parallel imports, OTC; switching strategies	
13.9	Health Technology Assessments (HTA) including meta-analyses and systematic reviews; health economics evaluation studies	
SECTION 14. Therapeutics		
14.1	Major therapeutic areas: epidemiology, pathophysiology, diagnosis and treatment	
14.2	Major areas of unmet medical need: epidemiology, pathophysiology, diagnosis and treatments	

14.3	Major drug classes, including small molecules, biologicals, advanced therapies: mode of action, use, safety, benefit-risk balance	
14.4	Gene therapy, somatic cell therapy, tissue, medical devices, device-drug combinations, vaccines: mode of action, use, safety, benefit-risk balance	
14.5	Drug-related Diagnostics	
14.6	Prescribing for particular populations e.g. children, elderly, pregnant and breast-feeding women, patients with renal or hepatic impairment	
14.7	Drug interactions	
14.8	Controlled drugs, drug abuse and drug dependence	
14.9.	Overdose and treatment of poisoning	
14.10	Therapeutic drug monitoring	