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	

PHARMATRAIN BASE COURSE **MODULE M1a (INT): INTRODUCTORY PROGRAMME**
LEARNING OUTCOMES
At the end of this Module the student should be able to demonstrate an understanding of the:
1. Process of drug development and identity of critical factors and decision points.
2. Importance of the patient in drug development.
3. Background to the development of the regulation of medicines and the role of the competent authorities.
4. Monitoring of drug safety.
5. Principles and practice of medical marketing.

PHARMATRAIN BASE COURSE **MODULE M1b: PRINCIPLES OF DISCOVERY OF MEDICINES AND DEVELOPMENT PLANNING**
LEARNING OUTCOMES
At the end of this Module the student should be able to demonstrate an understanding of the:
6. Role of pathophysiology and molecular biology-based pharmacology in drug development.
7. Principal steps in discovering, modifying, assessing and patenting new chemical and biological compounds (including advanced therapies) according to their therapeutic indication.
8. Resource planning (in terms of project management, budgeting and cost-control) involved in the management of a drug development programme.
9. Principles of translational research and its role in drug development.
10. Functions and elements (including business aspects) involved in the integrated development of a new drug.

MODULE 1a (INT): INTRODUCTORY PROGRAMME			
INT	**CURRICULUM CONTENT**	**LEARNING OUTCOMES MAPPING**	**SYLLABUS MAPPING**
INT1	Setting the scene: Medicines market overview and the Industry we are in.	1, 2, 3, 5	13.6, 13.8
INT2	Meeting the challenges of developing new, more effective, safer medicines.	1, 2, 3	
INT3	The highly regulated and ethical environment of medicines development.	1, 3	2.2, 8.1
INT4	The patient's view.	2	
INT5	The discovery process & non-clinical development.	1	
INT6	The target product profile (TPP) as the blueprint; satisfying the patients, doctors, regulators and payors.	1, 2, 3, 5	
INT7	A helicopter view of Integrated drug development including: attrition, orientation of the phases (0, 1, 2a, 2b, 3 & 4); modern approaches (learn, confirm), and conditional approvals.	1	
INT8	Exploratory Development: translational medicine; predictive science and personalised health care.	1, 2	
INT9	Confirmatory Development.	1, 2	
INT10	Principles of drug regulation and approval.	3	
INT11	Patient safety, pharmacovigilance and pharmacoepidemiology.	4	
INT12	The payors, market support activities and health economics.	5	

MODULE 1b: PRINCIPLES OF DISCOVERY OF MEDICINES AND DEVELOPMENT PLANNING			
M1	**CURRICULUM CONTENT**	**LEARNING OUTCOMES MAPPING**	**SYLLABUS MAPPING**
M1.1	Strategy and organisation of research including collaborative approaches e.g. with academia.	10	1.1
M1.2	Disease models; target identification, validation and selection. Principle steps in discovering, modifying, assessing and patenting new chemical and biological compounds.	7	1.2, 1.4
M1.3	Pathophysiology and molecular biology-based pharmacology. Molecular-based approaches: agonists, antagonists, enzyme inhibitors; genomics, proteomics, epigenetics.	6	1.3, 3.1
M1.4	Chemical and biological medicinal agents, natural medicines, medicine-coupled devices and advanced therapies.	6, 7	1.5
M1.5	Lead optimisation and development candidate selection; testing for biological activity.	7	1.6, 1.7
M1.6	Principles of translational medicine: relationship between animal and human pharmacology, molecular biological and physiological approach e.g. biomarkers, functional imaging, modelling and simulation.	9	1.8, 1.9
M1.7	Global integrated development of new medicines, including quality management.	10	2.1, 2.2, 2.5
M1.8	Project management techniques: central role of development plan, project teams, tools and decision-making from target product profile (TPP) and target product claims (TPC) to registration dossier submission. Resource planning, budgeting and cost control, in- and out-sourcing.	8	2.3, 2.7
M1.9	Development programme planning for small and / or special populations.	7	2.4
M1.10	R&D portfolio planning; in- and out-licensing of medicines.	10	2.6
M1.11	Therapeutic Topic 1		14.1 – 14.10
M1.12	Therapeutic Topic 2		14.1 – 14.10

PHARMATRAIN BASE COURSE **MODULE 2: NON-CLINICAL, PHARMACEUTICAL AND EARLY CLINICAL DEVELOPMENT**
LEARNING OUTCOMES
At the end of this Module the student should be able to demonstrate an understanding of the:
1. Choice and predictive value of the non-clinical testing programme as part of the overall drug development plan for chemical and biological compounds.
2. Integration of non-clinical tests into the overall drug development plan (including scheduling of toxicology tests with respect to clinical trials).
3. Steps in the pharmaceutical development of a drug substance and final drug product (including chemical and biological compounds).
4. Planning of clinical trial supplies for test substance and comparators (active and placebo).
5. Overview of non-clinical study requirements prior to First-into-Man studies.
6. Molecular and cellular basis of toxic reactions.
7. Principles and practical application of pharmacokinetics and toxicokinetics.
8. Early exploratory development in man.
9. Principles of clinical pharmacology and their application to clinical development.
10. Influence of genetic factors in drug development and drug response.

MODULE 2: NON-CLINICAL TESTING, PHARMACEUTICAL AND EARLY CLINICAL DEVELOPMENT			
M2	**CURRICULUM CONTENT**	**LEARNING OUTCOMES MAPPING**	**SYLLABUS MAPPING**
M2.1	Principles of non-clinical testing: differences and similarities between small molecule and biological macromolecule active agents and between the pharmacology and toxicology of compounds and their metabolites in animals and man, and their qualitative and quantitative assessment.	1	3. 2, 3.3
M2.2	Descriptive and quantitative *in vitro* and *in vivo* testing of new compounds; the choice and predictive value of these tests for acute, chronic, reproductive, genetic and immune toxicology, and carcinogenicity.	1	1.7, 3.4, 3.5

M2.3	Common mechanisms of damage to organs: their detection and elucidation. Molecular and cellular basis of toxic reactions.	6	3.6
M2.4	The scheduling of toxicology tests linked to development plans, regulatory needs, human and animal pharmacology, and to intended clinical uses and route(s) of administration. The size, cost and administration of the toxicology programme, its data management, quality assurance and report writing.	2	3.7, 3.8
M2.5	The continuous review of toxicology, its inclusion into clinical trial protocols, and investigator brochures, and the planning and correlation with the clinical evaluation of potential and observed toxicity in patients.	2	3.9
M2.6	Safety pharmacology; hypersensitivity	6	3.10
M2.7	Absorption, Distribution, Metabolism, Elimination (ADME); *in vitro* & *in vivo* study of metabolism; Toxicokinetics.	7	3.11
M2.8	Pharmaceutical development of *drug substance* (small chemical molecules or biological macromolecules) and up-scaling: manufacture and supply of materials; stability and storage; purity; compatibility; disposal.	3	4.1
M2.9	Pharmaceutical development of *drug product* and up-scaling: formulation(s); manufacture and supply of materials; labelling and presentation; stability and storage; purity; compatibility; disposal.	3	4.1, 4.2
M2.10	Choice of formulations and delivery systems depending on characteristics of compound and intended uses; testing formulations leading to a final specification, including bioequivalence.	3	4.3, 4.4
M2.11	Safety specification; pharmacopoeias.	3	10.20, 10.22
M2.12	The concept of blinding: preparing matching placebo and comparator products. Planning clinical trials supply requirements; packaging and labelling of clinical trial supplies (including stability and storage requirements); distributing supplies and disposing of remaining stocks.	4	4.5, 4.6, 7.14
M2.13	Assessment of non-clinical data and risk as prerequisites before administration to man: description of intended	5, 7	5.1, 5.2

	therapeutic indications, biomarkers, surrogate endpoints and criteria for 'go' 'no-go' decisions.		
M2.14	The early clinical development plan: objectives, design, conduct and analysis; tolerability, metabolism, pharmacokinetics, pharmacodynamics and safety in man; risk mitigation strategies; first-into-man studies, including exploratory strategies (Phase 0).	8	5.3, 5.4
M2.15	Clinical pharmacodynamics and pharmacokinetics: ADME; determinants of PK parameters; bioavailability and bioequivalence; extrinsic and intrinsic factors affecting drug metabolism (e.g. drug-drug, drug-food, drug-disease interactions).	9	5.5, 5.6, 5.7, 5.8
M2.16	Pharmacogenetics, pharmacogenomics, population pharmacokinetics, genetic factors influencing PK, PD and response to therapy. Personalised medicine.	10	5.9, 5.10
M2.17	Applicability of pharmacokinetics to dosage regimen and study design. Pharmacokinetic / pharmacodynamic modelling and simulation.	9	5.11
M2.18	Therapeutic Topic 3		14.1 – 14.10
M2.19	Therapeutic Topic 4		14.1 – 14.10

PHARMATRAIN BASE COURSE

MODULE 3: CLINICAL DEVELOPMENT OF MEDICINES: EXPLORATORY AND CONFIRMATORY

LEARNING OUTCOMES

At the end of this Module the student should be able to demonstrate an understanding of:

1. Early studies in patients: dose-finding / proof of concept studies and their impact on drug development plan.
2. Clinical trial design (including legal, regulatory, ethical and practical aspects): international differences.
3. Principles and application of statistics in clinical trials.
4. Procedures for clinical trial data collection (paper and electronic) and data management (including validation processes) to ensure optimal quality data.

5. Key strategic issues in the clinical trial process, in terms of legislative requirements and Good Clinical Practice (GCP).
6. The role of the investigator drug brochure (IDB).
7. Principles and practical relevance of ethical issues in biomedical research.
8. Legal and ethical provisions for protection of clinical trial subjects.

MODULE 3: CLINICAL DEVELOPMENT OF MEDICINES: EXPLORATORY AND CONFIRMATORY			
M3	**CURRICULUM CONTENT**	**LEARNING OUTCOMES MAPPING**	**SYLLABUS MAPPING**
M3.1	First administration to patients; principles of proof of concept and dose-finding studies.	1	5.12
M3.2	Concept of blinding.	2	4.5
M3.3	Trial design: pre-trial decisions and specifications; literature review; incidence and prevalence of the disease; risk factors; confounding variables; dealing with confounding factors and bias.	2	9.8, 9.25, 9.11, 9.20, 9.24
M3.4	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.	2, 5	10.10
M3.5	Protocol writing: detailing choice of location(s), trial design, blinding, placebo or other comparators, end-points, patient population, informed consent, sample size, randomisation, statistical methods, interim analysis.	2, 3	7.6
M3.6	Analysis of efficacy endpoints & of safety (intention to treat principles, handling of missing data etc.); interim analysis; statistical tests (sensitivity and specificity of tests; paired and non-paired tests, parametric and non-parametric tests, confidence limits).	3	9.14, 9.15, 9.16, 9.18, 9.19
M3.7	Options for data collection (manual and electronic) and standardisation; creation, maintenance and security of databases, software validation and archiving.	4	9.1, 9.3
M3.8	Case report form (CRF) design and review.	4	9.2
M3.9	The purpose and fundamentals of statistics. The role and responsibilities of the statistician. Statistical considerations of study design: hypothesis testing (the Null hypothesis, type I and type II error, significance, power),	3	9.5, 9.6, 9.7, 9.9, 9.10, 9.11, 9.15

	randomisation, sample size. The Statistical Analysis Plan (SAP), including interim analysis.		
M3.10	Principles of Good Clinical Practice and procedures applied in all stages of the clinical trial process to ensure subject protection, scientific validity and safety. Clinical trial registries.	5	7.4, 7.11
M3.11	Investigator Brochure: content, review and maintenance.	6	7.5
M3.12	Ethics: principles, history including Declaration of Helsinki, EU Directive 2001/20/EC, ethical review process, informed consent, safety and human dignity of research subjects. Ethical issues in biomedical research and pharmaceutical medicine.	7	8.1, 8.2
M3.13	Protection of research subjects. Risks, benefits and burden of study participation. Minimising risk including site qualification assessment; ethical aspects of subject contact and recruitment, and of reimbursement, compensation and inducement; indemnity and insurance for participants, investigators, institutions; complaint procedures.	7, 8	8.3, 8.6, 8.7, 8.8, 8.11
M3.14	Ethical aspects of research questions and study designs for first-in-human to post-marketing and epidemiological studies, including post-study follow-up procedures, placebo and comparator choice.	7, 8	8.4, 8.12
M3.15	Conflict of interest and equipoise.	8	8.5
M3.16	The informed consent process. Privacy, confidentiality and data protection.	7, 8	8.9, 8.10
M3.17	Ethical aspects of taking trial samples for genomic and related analyses.	8	8.13
M3.18	Ethical aspects of clinical trials in vulnerable populations.	8	8.14
M3.19	Ethical aspects of advanced therapy medicinal products.	8	8.15
M3.20	Ethical aspects of international clinical trials, considering socio-cultural differences.	8	8.16
M3.21	Therapeutic Topic 5		14.1-14.10
M3.22	Therapeutic Topic 6		14.1-14.10

PHARMATRAIN BASE COURSE **MODULE 4: CLINICAL TRIALS**
LEARNING OUTCOMES
At the end of this Module the student should be able to demonstrate an understanding of the:
1. Various types of clinical studies and the methods used to choose the appropriate design.
2. Main statistical methods used in clinical research.
3. Key issues involved in the conduct of a clinical study including investigator and site recruitment, investigative site management and conflict resolution.
4. Collection, evaluation and reporting of adverse event data in clinical trials.
5. Various quality management issues in clinical trials.
6. Impact of emerging results on the drug development plan.
7. Key operational and strategic issues in the clinical development plan.
8. Evaluation of the outcome of drug development: final therapeutic profile / usage of a medicine.
9. Role of the Target Product Profile (TPP) and Target Product Claims (TPC).
10. Role of the Drug Safety Monitoring Board (DSMB) and other relevant study committees.
11. Statistical issues in statistical report writing.
12. Evaluation and interpretation of clinical trial results.
13. Principles and practical application of critical appraisal.

MODULE 4: CLINICAL TRIALS			
M4	**CURRICULUM CONTENT**	**LEARNING OUTCOMES MAPPING**	**SYLLABUS MAPPING**
M4.1	Choice of interventional clinical trial design, of placebo and other comparators, of patient populations, of locations. New trial designs e.g. adaptive design. Non-interventional / observational study design.	1	7.1, 7.2, 7.3
M4.2	Types of data and standardisation of measurement e.g. handling of rating scales, including visual analogue scales, patient diaries and laboratory values. Statistical analysis of efficacy end-points and of safety.	2	9.12, 9.13, 9.14, 9.17

	Patient-reported outcomes e.g. diaries; quality-of-life measures		
M4.3	Feasibility testing and investigator recruitment; pre-study visits and investigator meetings; investigator training; contractual arrangements with investigators and contract research organisations, including matters such as publication rights and conflicts of interest.	3	7.7, 7.8, 7.10
M4.4	Project management: EUDRACT, CTA and ethics opinion, resources and budget, timelines, conflict resolution (e.g. investigator discontinuation).	3	7.9
M4.5	Clinical trial conduct / Investigative site management: Trial Master File (TMF), monitoring and source document verification, study medication handling and drug accountability. Within-trial decisions (e.g. code-breaking, premature termination); emergency coverage.	3	7.12, 7.13, 7.14, 7.15, 7.16, 7.17
M4.6	Quality management: quality assurance and quality control; SOPs; audits; inspections.	5	7.18
M4.7	Fraud and misconduct in biomedical research and clinical development.	3, 5	8.17
M4.8	Assessment and classification of adverse events (AEs), adverse drug reactions (ADRs), serious adverse events (SAEs) and suspected unexpected serious adverse reactions (SUSARs); evidence for association and causality.	3, 4	11.2
M4.9	Collection of adverse events in clinical trials; role of sponsors and investigators in reporting; regulatory requirements.	3, 4	11.4, 11.5
M4.10	Impact of results on the drug development plan (DDP) and possible need for further toxicology / pharmaceutical development data; regulatory review of existing and emerging research results.	6	5.13, 6.6
M4.11	Final definition of therapeutic indications. Categories of patients, delivery system(s), dosage forms and dosage regimens.	8	6.1
M4.12	Planning and global coordination / harmonisation of pre- and post-licensing clinical trial programmes; use of non-clinical and existing clinical trial data.	7	6.2
M4.13	Decision points, schedules & resources required for confirmatory clinical development plan (CDP). Calculation of clinical trial supplies and costs up to registration.	7	6.3, 6.4

M4.14	Review and maintenance of Target Product Profile (TPP) and Target Product Claims (TPC).	9	2.3
M4.15	The role of the independent Drug Safety Monitoring Board (DSMB) and other relevant study committees.	10	7.13
M4.16	Measurement and types of data; monitoring of clinical trials; source document verification, CRF review and correction, data entry, query generation and resolution, coding of adverse events, database lock.	2, 4	7.16, 9.4
M4.17	Preparing the statistical report: interpretation of analyses; assessment of violations, withdrawals, errors, bias; data manipulation, transformation and merging.	11	9.21, 9.22
M4.18	Clinical interpretation of study analyses and results. The Clinical Trial Report.	12	7.19, 9.23
M4.19	Critical review of publications.	13	9.25
M4.20	Therapeutic Topic 7		14.1-14.10
M4.21	Therapeutic Topic 8		14.1-14.10

PHARMATRAIN BASE COURSE **MODULE 5: REGULATORY AFFAIRS; DRUG SAFETY & PHARMACOVIGILANCE**
LEARNING OUTCOMES
At the end of this Module the student should be able to demonstrate an understanding of:
1. General principles of medicines regulation (both pre- and post-approval) at EU and global level.
2. Impact of medicines legislative requirements on regulatory activities within a pharmaceutical company.
3. Role of national agencies and international bodies in medicines regulation.
4. National provisions for management of (1) off-label / unlicensed use of medicines (2) controlled drugs.
5. Place of International Conference on Harmonisation (ICH) in medicines regulation (including Common Technical Document [CTD]).
6. Regulatory processes in the EU / EEA areas.
7. Regulation and legal considerations of Product Information.

8. Principles and practical application of medical devices regulation.
9. Roles of the various stakeholders (including pharmaceutical and other healthcare professionals, investigators, regulatory authorities) in drug safety and pharmacovigilance.
10. Classification of adverse events / adverse drug reactions.
11. Safety reporting requirements (according to the type of adverse event / reaction) pre- and post-approval.
12. Ongoing management of drug safety issues pre- and post-approval (including Risk Management Plans [RMPs], Periodic Safety Update Reports [PSURs]); ongoing benefit / risk assessment throughout the life-cycle of a medicine.
13. Role of pharmacoepidemiology in the life-cycle management of a medicine.
14. Factors influencing medication safety from the perspective of each stakeholder.

MODULE 5: REGULATORY AFFAIRS; DRUG SAFETY & PHARMACOVIGILANCE			
M5	**CURRICULUM CONTENT**	**LEARNING OUTCOMES MAPPING**	**SYLLABUS MAPPING**
M5.1	General principles of medicines regulation; philosophy of regulatory oversight; input of international bodies; evolution of control mechanisms; general differences between agencies; International Conference on Harmonisation (ICH).	1, 5	10.1, 10.2, 10.3, 10.4
M5.2	Overview of relevant regulatory Directives; overview of Good Practices (e.g. GCP, GMP, GLP) including inspections.	1	10.5
M5.3	Integration of regulatory affairs in pre- and post-marketing company activities; planning and reviewing product strategy. Prescription-Only-Medicines (POM) and Over-The-Counter (OTC) medicines; OTC switching strategies. Generics and biosimilars. Parallel imports.	2	10.6, 10.16, 13.10
M5.4	Common Technical Document (CTD & eCTD). Overviews; aggregate clinical trial report reviews, including annual reports and CTD summaries.	5	10.11, 10.12

M5.5	Regulatory systems in Europe, US, Rest of the World (ROW), and local special regulatory requirements. The preparation and submissions of marketing authorisation applications in major countries.	1, 2, 3	10.9, 10.13
M5.6	Approval, appeals and referral processes in Europe (Centralised Procedure, Mutual Recognition Procedure, Decentralised procedure, national procedures); updating and maintaining Marketing Authorisations (variations regulation); aspects of confidentiality and transparency.	6	10.7
M5.7	Regulation of Product Information: Summary of Product Characteristics (SmPC), labelling, US Prescribing Information, EU Patient Leaflet; EU readability testing.	7	10.14
M5.8	National differences in regulations / procedures for using locally unlicensed medicines (e.g. compassionate use). Off-label use and misuse.	4	10.17, 10.26
M5.9	Controlled drugs regulation.	4	10.25
M5.10	Medical device regulation.	8	10.19
M5.11	Risk management; EU Detailed Description of Pharmacovigilance System (DDPS); EU Risk Management Plan (RMP); Risk Evaluation and Mitigation Strategies (REMS) in the USA.	12	10.21
M5.12	The role of the pharmaceutical professional in drug safety and pharmacovigilance.	9	11.1
M5.13	The concept of benefit / risk assessment. Assessment and classification of adverse events (AEs), adverse drug reactions (ADRs), serious adverse events (SAEs) and suspected unexpected serious adverse reactions (SUSARs); evidence for association and causality.	10, 12	11.2, 11.3
M5.14	Risk factors for adverse events.	14	11.6
M5.15	Spontaneous reporting of suspected adverse drug reactions in the post-licensing phase.	11	11.7
M5.16	Dosage, drug accumulation, medication errors and interactions.	14	11.8
M5.17	Drug adherence / compliance.	14	11.9
M5.18	Periodic Safety Update Reports (PSURs).	11, 12	11.10
M5.19	Pharmacoepidemiology; main sources of epidemiological pharmacovigilance information.	13	11.11, 11.12
M5.20	Signal detection, interpretation and management.	12	11.13

M5.21	Post-Authorisation Safety Studies (PASS).	12, 13	11.14
M5.22	Post-authorisation risk management including issue and crisis management, risk communication with all the stakeholders; Direct Healthcare Professional Communication (DHPC).	12	11.15. 11.16
M5.23	Product withdrawal procedures; product defects and recall.	12	10.18, 10.24
M5.24	Therapeutic Topic 9		14.1-14.10
M5.25	Therapeutic Topic 10		14.1-14.10

PHARMATRAIN BASE COURSE **MODULE 6: HEALTHCARE MARKETPLACE; ECONOMICS OF HEALTHCARE**
LEARNING OUTCOMES
At the end of this Module the student should be able to demonstrate an understanding of:
1. Life-cycle activities (clinical, regulatory and marketing).
2. Processes of production and review of product information to ensure adherence to ethical and legal principles pertaining to marketing activities (Good Promotional Practice).
3. Role of patient organisations.
4. Principles and practical application of health economics and patient-reported outcomes within the pharmaceutical industry.
5. Principles of health technology assessment (HTA) and its role in thew upply of medicines to the marketplace.
6. Principles and practice of marketing within the pharmaceutical industry.
7. Drug budget control; pricing mechanisms.

MODULE 6: HEALTHCARE MARKETPLACE; ECONOMICS OF HEALTHCARE			
M6	**CURRICULUM CONTENT**	**LEARNING OUTCOMES MAPPING**	**SYLLABUS MAPPING**
M6.1	Life-cycle management planning: extension of therapeutic claims, new formulations, new dosage schedules by peri-marketing trials, post-marketing (surveillance) studies, OTC studies and quality of life measures.	1	6.5, 13.4, 13.10

M6.2	Information, promotion and education; information to patients, prescribing and patient compliance. Direct Healthcare Professional Communication (DHPC).	2	10.23, 12.1
M6.3	Advertising and promotion regulations; advertising claims: ethics, control and approval; promotional materials; Codes of Practice; promotional policy & procedures; Good Promotional Practice; promotional material and product support on the basis of the Marketing Authorisation.	2	10.5, 12.2, 12.3, 12.4, 12.5
M6.4	Role of patient organisations.	3	12.1
M6.5	Overview of healthcare economics, health economic evaluation studies. Principles of pharmacoeconomics and evidence based medicine. Measurement of healthcare efficiency. Governmental policy and third party reimbursement.	4	13.1, 13.2, 13.3, 13.7, 13.11
M6.6	Evidence Based Medicine (EBM), Health Technology Assessment (HTA), treatment Guidelines.	4	13.11
M6.7	Quality of Life, concept and measurement instruments.	5	13.4
M6.8	Principles and practice of marketing; market structure and competition; market analysis; medical marketing and market access. Economics of industry: competition, licensing, co-marketing.	6	13.5, 13.6, 13.8
M6.9	Publication strategy; educational meetings; sponsored meetings and publications.	2	12.6, 12.8
M6.10	Sales representative training; material and aids.	2	12.7
M6.11	Drug budget control; pricing mechanisms; methods of reimbursement.	7	13.1, 13.5
M6.12	Therapeutic Topic 11		14.1-14.10
M6.13	Therapeutic Topic 12		14.1-14.10