Section Overview

1. SECTION 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. herbal and other natural products, drug-coupled devices and advanced therapies
   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

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1.9 Relationship between animal and human pharmacology, molecular biology and physiology e.g. biomarkers, functional imaging, modeling and simulation

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. women, elderly, paediatrics, orphan drugs
2.5 Programmes in developing countries
2.6 R&D portfolio planning including in- and out-licensing of medicines (business development)
2.7 Resource planning: budgeting and cost control

3. Non-Clinical Testing
3.1 Pathophysiology- and molecular biology-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
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

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 prerequisites 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 Extrinsic and intrinsic factors

5.9 Population pharmacokinetics

5.10 Pharmacogenetics / pharmacogenomics

5.11 Applicability of pharmacokinetics to dosage regimen and study design

5.12 First administration to patients: principles of proof-of-concept and dose-finding studies

5.13 Impact of results on planned therapeutic indications, on predicted dosage schedule, on additionally required animal toxicology and on drug delivery concepts / forms

6. **Confirmatory Development: Strategies**

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

7. **Clinical Trials**

7.1 Choice of trial design, of placebo and of 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 Brochure: content, review and maintenance

7.6 Protocol preparation 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 Within-trial decisions e.g. code-breaking, interim analysis, premature termination

7.14 Study medication handling and drug accountability

7.15 Adverse event assessment and reporting; emergency coverage

7.16 Monitoring and source document verification

7.17 Trial master file (TMF)

7.18 Quality management system; SOPs; quality assurance and quality control; independent audits; inspections

7.19 Clinical trial report

8. **Ethics and Legal Issues**

8.1 Ethical issues in biomedical research and pharmaceutical medicine

8.2 Ethics: principles, history including 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 including 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 of subject contact and recruitment
8.7 Ethical issues of 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 and insurance for participants, investigators, institutions; complaint procedures
8.12 Ethical aspects of study follow-on
8.13 Ethical aspects of taking trial samples for genomic and related analyses
8.14 Ethical aspects of clinical trials in vulnerable populations
8.15 Ethical aspects of advanced therapy medicinal products
8.16 Ethical aspects of clinical trials in third world and emerging countries
8.17 Fraud and misconduct in biomedical research and clinical development

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 The purpose and fundamentals of statistics
9.6 Role and responsibilities of the statistician
9.7 The statistical analysis plan
9.8 Trial design: pre-trial decisions and specifications; risk factors; confounding variables
9.9 Hypothesis testing: the null hypothesis, Type I and Type II error, significance, power
9.10 Sample size calculation
9.11 Minimising bias
9.12 Types of data and standardisation of measurement
9.13 Patient-reported outcomes e.g. diaries; quality of life measures
9.14 Statistical analysis of efficacy end-points and of safety
9.15 Interim analysis
9.16 Paired and non-paired tests, parametric and non-parametric tests, confidence limits
9.17 Handling of rating and visual analogue scales, patient diaries and laboratory values
9.18 Handling of missing data  
9.19 Sensitivity and specificity of tests  
9.20 True and apparent incidence and prevalence  
9.21 Interpretation of analyses; assessment of violations, withdrawals, errors, bias  
9.22 Statistical principles and issues in statistical report writing: data manipulation, transformation and merging; preparation of the statistical report  
9.23 Clinical interpretation of trial results  
9.24 Dealing with confounding factors and bias  
9.25 Critical review of publications  

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 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, paediatrics, advanced therapies, generics and biosimilars  
10.9 Regulatory management systems in Europe, US, Japan, ROW and local special regulatory requirements  
10.10 Clinical Trials regulations; EU Directives and Guidelines 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 Aggregate clinical trial report reviews, including annual reports and Common Technical Document (CTD) summaries  
10.13 The preparation and submission of marketing applications in major countries (MAA, NDA, JNDA, CNDA)  
10.14 Product Information regulation: Summary of Product Characteristics; Package Insert; Patient Information Leaflets; Prescribing Information  
10.15 Advertising and promotion regulation: promotional material  
10.16 Prescription-only and over-the-counter medicines; switches  
10.17 Provisions for and use of unlicensed medicines  
10.18 Product defects and recall  
10.19 Medical device regulations
10.20 Pharmacopoeias
10.21 Risk management: Risk Management Plans (RMPs) in the EU; Risk Evaluation and Mitigation Strategies (REMS) in the USA
10.22 Safety Specification
10.23 Direct Healthcare Professional Communication
10.24 Product withdrawal procedures
10.25 Drug abuse and dependence
10.26 Off-label use and misuse

11. Drug Safety, Pharmacovigilance and Pharmacoepidemiology
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); evidence for association and causality
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; 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 Drug adherence / compliance
11.10 Periodic Safety Update Reports
11.11 Pharmacoepidemiology
11.12 Main sources of epidemiological pharmacovigilance information
11.13 Signal detection, interpretation and management
11.14 Post-authorisation safety studies
11.15 Post-authorisation risk management including issue and crisis management
11.16 Risk communication

12. Information, Promotion and Education
12.1 Information to patients and patient organisations, prescribing and compliance
12.2 Product Information content and preparation: Summary of Product Characteristics; Package Insert; Patient Information Leaflets; Prescribing Information
12.3 Product support and promotion
12.4 Codes of conduct: promotional policy and procedures; Good Promotional Practice
12.5 Advertising: claims, ethics, control and approval
12.6 Publication strategy
12.7 Sales representative training: material and aids
12.8 Educational meetings; sponsored meetings and sponsored publications

13. **Economics of Healthcare**
13.1 Principles of healthcare economics; principles of justice and equity in healthcare economics
13.2 Principles of pharmacoeconomics
13.3 Evidence Based Medicine; outcomes research
13.4 Quality of Life, concept and measurement instruments
13.5 Principles and practice of marketing; market structure and competition; market analysis, pricing and reimbursement strategies; national and local formularies
13.6 Medical marketing and market access
13.7 Measurement of healthcare efficiency, governmental policy and third party reimbursement
13.8 Economics of industry: competition, licensing, co-marketing
13.9 Financial control, return on investment, fixed assets, budgeting, accounting, profitability
13.10 Generics and biosimilars, parallel imports, OTC; switching strategies
13.11 Health Technology Assessment (HTA) including meta-analysis and systematic review; health economics evaluation studies

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