Faculty of Pharmaceutical Medicine

Advancing the science and practice of pharmaceutical medicine for the benefit of the public

Exam Specification

Certificate and Diploma in Pharmaceutical Medicine

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Version 9	August 2026	Dr Kristina Strutt MA MBBS MRCP FFPM GFMD Chair, Officers of the Board of Examiners Dr Danie du Plessis MD, MBA, PGCPLC, GFMD, FFPM Chair, Education and Standards Committee

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1 Background

This document outlines the format and content of the Diploma in Pharmaceutical Medicine (DPM) examination and forms the basis of both the setting of the examination, with respect to the types of papers, the number and range of questions asked, and the provision of feedback to candidates.

Candidates for the Certificate in Pharmaceutical Medicine (CPM) should note that the DPM Part 1 multiple choice question paper referenced in this document is also the Certificate in Pharmaceutical Medicine question paper.

2 Syllabus

With effect from 2012, the DPM exam uses the IMI PharmaTrain Syllabus (the Syllabus) for Pharmaceutical Medicine/Drug development Science. Version 3.0 (dated May 2024) will be used until further notice. A copy of the Syllabus is included as Appendix 1 to this document.

The Syllabus is divided into 13 sections, as shown in Table 1:

Table 1 Syllabus Sections

Section No	Section name
SECTION 1	Drug Discovery
SECTION 2	Development of Medicines: Planning
SECTION 3	Non-Clinical Testing
SECTION 4	Pharmaceutical Development and Manufacturing
SECTION 5	Exploratory Development: Molecule to Proof of Concept
SECTION 6	Confirmatory Development
SECTION 7	Clinical Trials
SECTION 8	Ethics and Legal Issues
SECTION 9	Data Management and Statistics
SECTION 10	Regulatory Affairs
SECTION 11	Patient Safety, Pharmacovigilance and Pharmacoepidemiology
SECTION 12	Medical Information, Education, Promotion: Communication Strategies and Channels
SECTION 13	Health Economics, Outcomes Research, Pharmacoeconomics and Patient Access

Within each Section are sub-sections which list in greater detail the knowledge items appropriate to that section.

3 Examination Structure

The Diploma is a two-part examination. Part 1* consists of a Multiple-Choice Question (MCQ) paper and Part 2 comprises a Short Answer Question (SAQ) paper and a Critical Appraisal Paper (CAP). Part 2 of the exam is held approximately 2 weeks after Part 1. Candidates must have passed Part 1 before they are eligible to sit Part 2. The two Part 2 papers are held within the same week, usually on consecutive days.

3.1 Part 1 Multiple Choice Questions

The MCQ paper* comprises 75 questions (stems) each with five completions such that a total of 375 discrete questions are asked. The completions relate directly to the stem and may be either true or false. Any number may be true and any number may be false. Candidates are required to indicate which are true and which false and are awarded 1 mark for each correct answer. Incorrect or missing answers score 0. There is no negative marking. Candidates have 2.5 hours to complete the paper.

Each of the 75 stems is assigned to one of the 13 syllabus sections shown in Table 1. The assignment will be made initially by the author of the question and will be verified by the examination review group (which is typically the Officers and Paper Conveners) before the use of the question in a sitting.

Where the question tests knowledge that is drawn from more than one section of the syllabus, it will be assigned to the section which has the majority of completions.

The ***minimum*** number of questions per section of the syllabus for the MCQ paper is shown in Table 2. As this is the minimum number it does not add up to 75. The balance will be made up with questions from any section.

*The Diploma Part 1 multiple choice question paper is also the Certificate in Pharmaceutical Medicine question paper.

Table 2 Allocation of questions within the MCQ paper according to syllabus sections

Section Number	Section Title	Minimum Number of Questions
SECTION 1	Drug Discovery	2
SECTION 2	Development of Medicines: Planning	1
SECTION 3	Non-Clinical Testing	5
SECTION 4	Pharmaceutical Development and Manufacturing	2
SECTION 5	Exploratory Development: Molecule to Proof of Concept	6

SECTION 6	Confirmatory Development	1
SECTION 7	Clinical Trials	9
SECTION 8	Ethics and Legal Issues	4
SECTION 9	Data Management and Statistics	5
SECTION 10	Regulatory Affairs	7
SECTION 11	Patient Safety, Pharmacovigilance and Pharmacoepidemiology	7
SECTION 12	Medical Information, Education, Promotion: Communication Strategies and Channels	3
SECTION 13	Health Economics, Outcomes Research, Pharmacoeconomics and Patient Access	3

3.2 Part 2 Short Answer Question Paper

For the SAQ paper, candidates have 2 hours and 30 minutes to answer 10 compulsory questions in note form.

Each of the 10 questions is assigned to one of the 13 syllabus sections shown in Table 1. The assignment will be made initially by the author of the question and will be verified by the examination review group (which is typically the Officers and Paper Conveners) before the use of the question in a sitting. For questions which require knowledge of more than one section of the syllabus, a primary section will be assigned according to the predominant theme of the question.

The SAQ paper will consist of at least one question from the following sections of the syllabus:

Section 1 or Section 3	Drug Discovery / Non-Clinical Testing
Section 5	Exploratory Development: Molecule to Proof of Concept
Section 7 or Section 8	Clinical Trials / Ethics and Legal Issues
Section 9	Data Management & Statistics
Section 10	Regulatory Affairs
Section 11	Patient Safety, Pharmacovigilance and Pharmacoepidemiology

Section 12 or Section 13	Medical Information, Education, Promotion: Communication Strategies and Channels / Health Economics, Outcomes Research, Pharmacoeconomics and Patient Access

The balance of the 10 questions will be drawn from all sections of the syllabus, including from the compulsory sections listed above. There will be no more than two primary questions from any one section.

3.3 Part 2 Critical Appraisal Paper

The CAP will require candidates to read a published manuscript and answer questions on the article. Two and a half hours are allowed for this paper. The questions will be of three broad types:

1. Descriptive questions. These require the candidate to summarise information or data that is given within the manuscript.

2. Comment/critique questions. These questions will require the candidate to comment in a critical way on information within the paper. A comment question will typically follow a descriptive question and will relate directly to it.

3. Questions relating to next steps, trial redesign etc. These questions will require the candidate to think beyond the paper they have in front of them and suggest alternative or follow-up study designs etc.

The total number of questions asked will vary from year to year according to the content of the manuscript but will typically be around 14-16. There will be a ***minimum*** of four questions from category 1, three questions from category 2 and one question from category 3. The remainder of the questions can be drawn from any category provided the split allows for the allocation of marks described below.

Approximately 35% (permitted range 35-45%) of the marks available for the paper will be assigned to descriptive (category 1) questions and the remainder of the marks will be awarded to questions from categories 2 and 3.

Questions asked in the CAP may come from any part of the *Syllabus*, and the mix of questions will vary from sitting to sitting according to the constraints of the particular manuscript chosen. However, at a ***minimum***, the manuscript chosen must allow at least one question from the following sections of the Syllabus to be asked:

Section 7	Clinical Trials
Section 8	Ethics & Legal Issues
Section 9	Data Management & Statistics

Ideally, the manuscript will also allow at least one question from Section 11, Patient Safety, Pharmacovigilance and Pharmacoepidemiology.

4 Feedback to Candidates

4.1 Passing Candidates

Candidates who pass either Part of the DPM examination will be informed by email that they have passed and will be provided with their overall marks for each of the papers that they sat.

4.2 Failing Candidates

Candidates who fail either Part of the DPM examination will be informed by email that they have failed and will be provided with their overall marks for each of the papers which they sat. In addition, to assist these candidates with preparation for future examinations, more detailed feedback will be provided on their performance in the different sections of the syllabus.

The candidate's performance in the MCQ paper will be fed back by means of completion of the following table (Table 3) for each candidate individually:

Table 3 Feedback table for MCQ paper

Syllabus Section Number	**Syllabus Section**	**Number of Questions from this Section**	**Total possible score for questions in this section** (= no. of qu x 5)	**Candidate's score for this Section**
1	Drug Discovery			
2	Development of Medicines: Planning			
3	Non-Clinical Testing			
4	Pharmaceutical Development and Manufacturing			
5	Exploratory Development: Molecule to Proof of Concept			
6	Confirmatory Development			
7	Clinical Trials			

8	Ethics and Legal Issues			
9	Data Management and Statistics			
10	Regulatory Affairs			
11	Patient Safety, Pharmacovigilance and Pharmacoepidemiology			
12	Medical Information, Education, Promotion: Communication Strategies and Channels			
13	Health Economics, Outcomes Research, Pharmacoeconomics and Patient Access			

The candidate's performance in the SAQ paper will be fed back by means of completion of the following table (Table 4) for each candidate individually:

Table 4 Feedback table for SAQ paper

Question Number	Syllabus Section^	Candidate's Score (Out of 10)
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
^Section of the Syllabus to which the question primarily relates		

For the CAP, candidates will be notified of their marks for each of the questions individually, as shown in Table 5.

Table 5 Feedback table for CAP paper

Question Number	Number of marks available	Candidate's Score
1		
2		
3		
4		
5		
6		
etc		

5. Review

The examination specification will be kept under informal review on a continual basis by the Officers of the Board of Examiners and Paper Conveners group. In addition, it will undergo a formal review at any time that there is a change in the Syllabus or a change in structure or conduct of the examination. Changes may be made to the specification following either type of review.

6. Approval

The Examination Specification will be approved by the Chairs of the Board of Examiners and the Education and Standards Committee who will sign off the document on behalf of the two bodies following appropriate review and approval by those two bodies.

PharmaTrain Syllabus 2024 V3.0

Pharmaceutical Medicine/Medicines Development Science

Jointly developed by:
PharmaTrain Federation; Faculty of Pharmaceutical Medicine; International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine.

SYLLABUS SECTIONS

Section 1: Drug Discovery

Section 2: Development of Medicines: Planning

Section 3: Non-Clinical Testing

Section 4: Pharmaceutical Development and Manufacturing

Section 5: Exploratory Development: Molecule to Proof of Concept

Section 6: Confirmatory Development

Section 7: Clinical Trials

Section 8: Ethics and Legal Issues

Section 9: Data Management and Statistics

Section 10 Regulatory Affairs

Section 11. Patient Safety, Pharmacovigilance and Pharmacoepidemiology

Section 12: Medical Information, Education, Promotion: Communication Strategies and Channels

Section 13: Health Economics, Outcomes Research, Pharmacoeconomics and Patient Access

Section 1. Drug Discovery

1.1. Unmet medical need; target compound / product profile and frameworks to build it. Target identification and validation.

1.2. Strategy, organisation and rationalisation of research including collaborations and co-development. The process of due diligence and in- and out-licensing.

1.3. Consideration of intellectual property rights.

1.4. The role of bioinformatics and artificial intelligence in drug discovery.

1.5. The role of medicinal chemistry, manufacturing and formulation in drug discovery. Dose form development. Made-to-order and on-site manufacture of pharmaceuticals.

1.6. Receptor-based approaches (agonists and antagonists), enzyme inhibitors; genomics, proteomics, metabolomics. Other therapeutic approaches: natural products, repurposing, drug delivery systems, drug-device combinations, antibody therapy, nanotechnology, nucleic acid therapies (antisense oligonucleotide therapy, RNA and DNA as medicines), vaccines, advanced therapies (gene editing, gene therapy, cell therapies, tissue engineering), stratified medicine, therapeutics for the microbiome.

1.7. The general principles of translational medicine. Translational principles for: public health interventions such as vaccines; pandemic situations such as the COVID-19 pandemic; product re-profiling. The translational development of microbiome-related products.

1.8. Hit-to-lead, lead optimisation and candidate compound selection for further development.

1.9. *In silico, in vitro* and *in vivo* testing of new compounds including disease models (*in vivo* and *in vitro*) development and relevance.

Section 2. Development of Medicines: Planning

2.1. Sourcing and securing sufficient available finance before commencement of any project in medical product R&D.

2.2. Resource planning; allocation of funding; budgeting and cost control mechanisms.

2.3. Project management techniques: drug development plan, project teams, tools and decision-making from target product profile to registration dossier submission and lifecycle management.

2.4. Programme-planning in special populations - amongst others, elderly and incapacitated people.

2.5. Paediatric development planning, a. for products indicated primarily for paediatric patients and b. for products developed for adults and requiring a paediatric investigation plan (PIP); orchestration of these parallel developments.

2.6. Programmes in economically developing countries.

2.7. R&D portfolio planning; in- and out-licensing of medicines. Medical due diligence.

Section 3. Non-Clinical Testing

3.1. Use of *in silico*, animal and cell-based models of disease mechanisms to study the actions of a new drug.

3.2. Differences in non-clinical safety and toxicity packages between small molecules, biological medicines, advanced therapies.

3.3. Non-clinical testing including the actions of medicinal products and their metabolites in animal, human and cell preparations that provide qualitative and quantitative assessment through genotoxicity, general toxicity, toxicokinetics, pharmacokinetics, drug metabolism, safety pharmacology, immunotoxicity, reproductive toxicity, carcinogenicity. Duration of studies to support clinical trials and marketing approval.

3.4. The purpose of descriptive and quantitative *in silico*, *in vitro* and *in vivo* non-clinical testing; the choice of appropriate tests for acute and chronic drug administration. The use of organoids.

3.5. The common mechanisms of drug-induced organ damage and dysfunction; detection and elucidation; pathological assessment e.g. structural staining and immune-histochemistry; functional assessment e.g. QTc interval testing, liver and lung function tests.

3.6. The scheduling of non-clinical testing linked to product development plans, regulatory requirements, human and animal pharmacology, intended clinical use and routes of administration.

3.7. The size, cost and management of the non-clinical testing programme; data management, quality assurance and reporting.

3.8. The regular review of non-clinical testing, its inclusion into clinical trial protocols and investigator brochures. Relevance of expert interpretation and presentation of non-clinical testing results in the investigator brochure. Appropriate planning and correlation with the clinical evaluation of potential and observed toxic effects in patients.

3.9. Safety pharmacology including drug hypersensitivity of both small and large molecules.

3.10. Toxicokinetics; *in vitro* and *in vivo* study of metabolism and pharmacokinetics, defining therapeutic margins.

3.11. The non-clinical study of biological medicines, vaccines, advanced therapies e.g. cell and gene therapies, tissue engineering.

3.12. Refining, Reducing, Replacing the use of animals in non-clinical testing. 3Rs programmes; their sustenance and development.

Section 4. Pharmaceutical Development and Manufacturing

4.1. Pharmaceutical development of drug substance and drug product, including biological medicines and advanced therapies: scalability, manufacture, supply and distribution of materials; labelling and presentation; stability and storage; purity; compatibility; disposal.

4.2. The economic primary production of new compounds and secondary production of research and market formulations.

4.3. The choice of formulations and delivery systems depending upon the characteristics of the compound and its intended uses.

4.4. The principles of *in vitro* and *in vivo* testing of formulations for bioequivalence, stability, impurity, incompatibility and acceptability for different populations leading to a final specification, including formulations of follow-on drugs - generics, biosimilars.

4.5. The non-clinical study of biopharmaceutical formulations; including excipients.

4.6. Planning clinical trial supply requirements; packaging and labelling of clinical trial supplies; stability and storage requirements; supply distribution; disposal of remaining stocks. Preparing matching placebo and competitor products.

4.7. Pharmacological standards; pharmacopoeias: role, use and hierarchy.

4.8. Manufacture of medicinal products including good manufacturing practice and good distribution practice. Manufacturing strategy and models. Quality by Design principles and drug manufacturing.

Section 5. Exploratory Development: Molecule to Proof-of-Concept (as defined by ICH)

5.1. Intended therapeutic indications and target product profile; biomarkers for target engagement, efficacy and safety end-points and criteria for ‘go’ / ‘no-go’ decisions for entry into humans and progression to proof-of-concept trials.

5.2. Assessment of non-clinical data and the risk of hazards as prerequisites before administration to humans; including the calculation of starting and maximum dose for a trial.

5.3. Phase 0 studies: exploratory microdose and subtherapeutic dose studies; the importance, limitations and uses of microdoses. Use of radio imaging for product distribution.

5.4. The early clinical development plan: from first-in-human to proof-of-concept, modelling and simulation, model-informed development, tolerability, metabolism, pharmacokinetics, pharmacodynamics. Safety in humans: risk mitigation and safety assessment in human studies; dose escalation safety committees; special considerations for the individual product.

5.5. Pharmacokinetics, ADME, pharmacokinetic / pharmacodynamic and pharmacokinetic / physiological models and special groups; intrinsic and extrinsic factors which affect the pharmacokinetics of a medicinal product; dosage and accumulation, use of

radiolabelled drug, bioavailability, bioequivalence and population pharmacokinetics; radiopharmaceuticals, dosimetry considerations.

5.6. Pharmacogenetics / pharmacogenomics.

5.7. First-in-human studies: patients and healthy volunteers; principles of proof-of-concept and dose-finding studies; starting dose and dose-escalation plan for first-in-human and early clinical studies, including applicability of pharmacokinetics to dosage regimen and study design in first-in-human studies and subsequent Phase II and Phase III clinical trials.

5.8. Biomarker and analytical method validation.

5.9. Studies for detailed dose-finding / dose-response relationship, effect size, treatment duration and conditions. Identification of the population / subgroup most profiting from the treatment; the most appropriate primary endpoint.

5.10. Impact of results on planned therapeutic indications, predicted dosage schedules and drug delivery concepts / formulations; additional non-clinical requirements; reformulation studies; new pharmacology studies; risk-prediction algorithms to assess safety risks and enable development of risk-management approaches to be applied during continued development.

5.11. Obtaining and implementing feedback from regulatory agencies and / or health technology assessment bodies on emerging research results and development plans through scientific advice procedures; consulting with other external bodies on proposed development plans (repeated as 6.6).

Section 6. Confirmatory Development

6.1. Options for the clinical development plan; asset risk assessment and mitigation; schedules and decision points for the confirmatory clinical development programme.

6.2. Translation of the defined target product profile into the confirmatory clinical development programme design; pivotal and other Phase III studies; selection of primary and secondary endpoints and comparators for Phase III clinical trials; final definition of therapeutic indications; risk minimisation measures for research participants.

6.3. Choice of countries / regions to participate in confirmatory clinical trials; patient numbers and selection criteria; delivery systems; dosage forms; dosage regimens; clinical trial supplies - ensuring all these aspects are appropriate for this stage of development.

6.4. Planning and global coordination including alignment of pre-licensing and post-licensing clinical trial programmes; permitted use of competitor class data, non-clinical data and existing clinical trial data.

6.5. Lifecycle management planning: label extension of therapeutic claims and new formulations.

6.6. Obtaining and implementing feedback from regulatory agencies and / or health technology assessment bodies on emerging research results and development plans through scientific advice procedures; consulting with other external bodies on

proposed development plans.

Section 7. Clinical Trials

7.1 Application of ICH Good Clinical Practice to clinical studies.

7.2. Choice of trial design: non-inferiority / superiority / other designs including cross-over; placebo / other comparators. Patient populations; sample size; international locations (global); randomisation; end-points; statistical analysis. PK and PD studies, first-in-human; specific. Encompass patient engagement and advisory meetings with national regulatory authorities.

7.3. New trial designs, adaptive designs, umbrella and basket trials, platform trials plus use of real world evidence studies in marketing authorisation. Consider use of digital and remote monitoring and broader use of patient-reported outcomes. Modelling and simulation use in trial design.

7.4. Post-authorisation clinical development: Phase IV clinical trials; non-interventional / observational studies; real-world evidence generation; post-authorisation studies versus line extensions; patient group registries; drug utilisation studies; cluster trials; treatment optimisation studies; re-purposing studies.

7.5. Investigator Brochure: content, review, update and maintenance; presentation and usage; regular ease of use of digital access and opportunity for revisions.

7.6. Protocol development and amendments: development of the case report form (including eCRF); understandable information for patient consent; suitability for collaborating parties; deviations and serious breaches of the protocol.

7.7. Clinical trial feasibility and investigator recruitment; pre-study visits; investigator meetings and investigator training, including virtual as well as face-to-face meetings, on-line report forms; cover all site personnel as much as possible with virtual meetings. Site qualification assessment.

7.8 Contractual arrangements with investigators, sponsors, co-sponsors, patient advocacy groups, academic institutions / hospitals, contract research organisations, site management organisations; publication rights considering co-development partners. Vendor management.

7.9 Clinical trial management from sponsor and site perspective including risk identification and management.

7.10 Clinical trial registries; requirement to follow the general data protection regulation (GDPR) or equivalent. Transparency in clinical trials: from study to register to publication.

7.11 Data and Safety Monitoring Committee; composition, independence, role in clinical research.

7.12 Within-trial decisions e.g. code-breaking, interim analysis, data and safety monitoring committee, independent safety monitor, premature termination; urgent safety measures.

7.13 Study medication handling and drug accountability.

7.14 Adverse event assessment and reporting; emergency coverage provision.

7.15 Monitoring and source document verification; evolution of clinical trial monitoring to include remote and digitalised data oversight and monitoring actions to be taken as appropriate; digital decentralised studies.

7.16 Trial Master File - patient information anonymised to ensure safety and anonymisation.

7.17 Risk-based quality management in clinical trials: Quality by Design, quality manual; standard operating procedures; quality assurance and quality control; independent audits; inspections.

7.18 Reporting of clinical trial data: data sharing and open data, transparency, aggregated clinical trial report review and annual clinical trial reports; apply with digital tools and include lay summary.

7.19 Consideration for special populations in clinical trials e.g. the elderly, pregnant women, extreme ages such as premature babies / neonates, incapacitated people; management of biological samples involved with gene therapy; respect of patients' rights. Consideration of ethics committee requests for continuance of new therapies after study completion for patient volunteers.

7.20 Medical device and drug-device combination trials are included alongside trials with medicinal products, as such trials now involve assessment of safety and efficacy. Developing trial registries.

7.21 Opportunities that arise from real time collection of data and challenges including verification and validation. Practical steps in transitioning to hybrid and decentralised trials with patient engagement. Consideration of in-home services, digital data acquisition, agile clinical monitoring, wearables, real-world data and specialised databases with patient-reported outcomes; use of artificial intelligence.

Section 8. Ethics and Legal Issues

8.1. Ethics: principles and history including Declaration of Helsinki, Belmont Report and other relevant ethical principles, directives and codes of practice applicable throughout the entire lifecycle of a medicine; ethics review, informed consent, safety and human dignity of research participants, role of ICH GCP and other Good Practices.

8.2. Upholding good ethical and professional standards in pharmaceutical medicine, for example avoiding and addressing fraud and misconduct; consistent application of ethical standards.

8.3 Sponsor and investigator responsibilities; avoidance of scientific and economic conflicts of interest.

8.4. Ethical and scientific integrity in research questions and study designs from first-in-human to post-marketing and epidemiological studies, including scientific rationale, statistical robustness, appropriate patient populations, comparators and choice of endpoints; ensuring equipoise in comparator clinical studies; consideration of conflicts of interest.

8.5. Ethical considerations in pharmaceutical medicine, including non-clinical studies, database searches, medicines' advertising, clinical trial participant contact, recruitment and reimbursement, use of social media, data protection, confidentiality and pharmacovigilance.

8.6. Informed consent process, including defining benefit-risk balance, requirements for study participation including for children and special populations for example elderly, emergency research, incapacitated people; additional consent for future use of collected trial data and biological samples; merging of data from multiple trials.

8.7. Privacy, data confidentiality, confidential treatment of biological samples and genetic data, standards for data protection, publication of clinical trial results.

8.8. Ethical aspects of clinical trial follow-on: continuation of study medication to study participants, pre-marketing authorisation, pre-reimbursement availability.

8.9. Ethical and legal aspects of clinical trials in special populations for example elderly, emergency care, incapacitated people, migrating populations; during crisis conditions for example human-made, natural and environmental disasters.

8.10. Environmental, social and governance factors relevant to medicines development and clinical trials; sustainability of clinical trials.

8.11. Ethical aspects of all parties involved in research of advanced therapies involving cell and tissue donation.

8.12. Ethical aspects of clinical trials in economically developing countries.

8.13. Ethical issues and cases in biomedical research and pharmaceutical medicine, for example the need for an ethics consensus on multi-professional teams, on corporate responsibility, on environmental sustainability.

8.14. Liability for harms; clinical trial indemnification; product liability post-marketing; personal and corporate negligence; whistleblowing and complaints procedures.

8.15. The importance and standards of transparency in clinical trials including reporting results for the professional community, and for patients and public in lay language.

Section 9. Data Management and Statistics

<u>Statistical aspects of study design.</u>

9.1. Fundamentals: randomisation, avoidance of bias, avoidance of missing data; estimand (concept), estimand framework; sample size calculation.

9.2. Interim analyses: efficacy, futility, safety.

9.3. Statistical aspects of dose-finding studies.

9.4. Equivalence and non-inferiority trials: rationale, choice of margin.

9.5. Adaptive designs: basic ideas including advantages, concerns, avoidance of statistical and operational bias.

Data management.

9.6. Data collection: including diaries.

9.7. Case report form design and completion; source data verification, query generation and resolution.

9.8. Data processing: data entry, coding of adverse events, medical history and concomitant medications; identification of protocol violations and deviations.

9.9. Risk-based approach to data quality.

9.10. Databases: maintenance, security, standardisation, streamlining the processes; Clinical Data Interchange Standards Consortium.

Statistical methods for analysis.

9.11. Fundamentals: probability; null and alternative hypotheses, type I and type II errors, p-values, confidence intervals, intention-to-treat, analysis sets.

9.12. Endpoints: endpoint types (continuous, binary / categorical, time-to-event, count), data transformation, primary and secondary and exploratory endpoints, dealing with multiplicity.

9.13. Specific methodologies: simple statistical tests (parametric and non-parametric), odds ratios, risk ratios, hazard ratios, Kaplan-Meier curves, rate ratios, modelling to correct for baseline imbalances and to reduce variation.

9.14. Equivalence and non-inferiority: confidence interval and p-value approaches, assay sensitivity.

9.15. Evaluating homogeneity: forest plots and subgroup evaluation, testing for interaction.

9.16. Dealing with missing data through imputation and modelling. Classification of missing data; missing completely at random, missing at random, missing not at random.

9.17. Bayesian statistics; basic ideas.

9.18. Safety data: tables and graphs for the evaluation of adverse events, laboratory data and other data relating to safety.

9.19. Diagnosis: sensitivity, specificity and introduction to Receiver Operating Characteristic curves.

9.20. Meta-analysis: distinction versus pooling, fixed and random effects mode, extension to network meta-analysis; critique of network meta-analysis.

9.21. Observational studies: propensity scoring, matching to minimise bias, inverse propensity score weighting.

The statistics process.

9.22. Content for the protocol statistical methods section and the Statistical Analysis Plan.

9.23. Writing the Statistical Study Report and contributing to the Clinical Study Report and clinical publications; to include the clinical interpretation of statistical analyses.

9.24. Data science: principles, practices, applications. Contribution of Data science to pharmaceutical development throughout the value chain from discovery to marketplace.

9.25. Data science and statistics: differences and similarities; interaction and separation; respective contributions (present and potential) to medicines development, regulation and use.

Section 10. Regulatory Affairs

10.1. Historical context for regulation; evolution of regulatory mechanisms in various countries; emergence and concept of regulatory science. Interaction of sponsor and regulator in the development and marketing of medical products.

10.2. Roles of international bodies and differences between them in regulation and standard setting: International Council on Harmonisation of Technical Requirements for Human Use (ICH); World Health Organisation (WHO), Council for International Organisations of Medical Sciences (CIOMS), International Coalition of Medicines Regulatory Authorities (ICMRA), World Medical Association (WMA), International Organisation of Standardisation (ISO), Organisation for Economic Co-operation and Development OECD. Reliance on, recognition of and cooperation with other regulatory authorities.

10.3. Good practices (GxPs) relevant to medicines development including good manufacturing practice, good laboratory practice, good clinical practice, good clinical laboratory practice, good vigilance practice, good documentation practice.

10.4. Developing a regulatory strategy to support the development lifecycle management of medicines, devices, combination products and diagnostics.

10.5. Integration of regulatory affairs into pre- and post-marketing; planning and review of product strategy.

10.6. Regulatory processes in Europe for the evaluation and approval of new medicinal products; scientific advice; appeal and arbitration procedures; procedures for maintaining, varying and cancelling European marketing authorisations; referrals processes; confidentiality and transparency.

10.7. Regulatory considerations for rare diseases, paediatrics, pregnancy, elderly, ethnic diversity, gender distribution, advanced therapies.

10.8. Regulatory processes: generics and biosimilars; how to substitute the innovator product.

10.9. Comparison of international regulatory systems: Europe, US, Japan, Africa, China, India and Rest-of-World; local special regulatory requirements.

10.10. European regulations and guidance for clinical trial application (CTA), maintenance and completion; EU single submission portal; substantial protocol modifications; transparency. Comparison of regulatory systems in international and relevant national territories.

10.11. Common technical document (CTD and e-CTD); clinical overviews; clinical summaries.

10.12. The preparation and submission of marketing applications in major regions e.g. marketing authorisation application (MAA, EU), new drug application (NDA, US), and national territories.

10.13. Product Information regulation: summary of product characteristics; package insert; patient information leaflets; differences in labelling including e-labelling.

10.14. Prescription-only and over-the-counter medicines; switches. Example: differences between US, UK, Australia and EU.

10.15. Regulatory provisions for the use of unlicensed medicines; off label use; different approaches in US and EU (IND versus named patient).

10.16. Safety concerns which lead to urgent safety restrictions, product restriction, suspension and withdrawal procedures; product defects and recall.

10.17. Medical device regulation including therapeutic and diagnostic devices, and in vitro diagnostics.

10.18. Regulation of natural products and relevant traditional medicines.

10.19. Risk management: risk management plan (RMP, EU); risk evaluation and mitigation strategies (REMS, US); additional monitoring of authorised medicines e.g. inverted black triangle (EU), black box warning (US). Options for suitability of conditional approvals, use of real-world data, additional monitoring and regulatory requests for further data submission.

10.20. Aggregate safety data reports: development safety update report (DSUR); periodic benefit risk evaluation report (PBRER).

10.21. Regulation and procedures for early access to medicines; named patient supply, compassionate use, PRIME procedure (EU); ACTU procedure (France); early access to medicines scheme (EAMS, UK).

10.22. Falsified and counterfeit medicines.

10.23. Post-authorisation efficacy and safety studies and treatment optimisation studies e.g. non-interventional / observational studies; investigator initiated studies; patient group registries; drug utilisation studies.

SECTION 11. Patient Safety, Pharmacovigilance and Pharmacoepidemiology

11.1. Roles and responsibilities of pharmaceutical professionals for patient safety and pharmacovigilance.

11.2 Assessment and classification of adverse events, adverse drug reactions, serious adverse events and suspected unexpected serious adverse reactions (SUSARs); evidence for association and causality at case level and at aggregated case assessment.

11.3. The concept of a structured integrative benefit-risk framework; patient involvement in strategy and assessment of risk mitigation and management approaches throughout the product lifecycle; documentation and review of benefit-risk assessment and risk management activities.

11.4. Collection of safety data in clinical trials including adverse events and adverse events of special interest. Approaches to, and planning for, data pooling across trials and analysis of safety in subpopulations. Safety data reporting requirements during clinical trials - serious adverse events, SUSARs, aggregate safety data reports. Safety implications of breaches of good clinical practice.

11.5. The role of investigators, clinicians, study monitors, sponsors and manufacturers in the pre- and post-marketing phases to detect, assess and report adverse events and suspected adverse drug reactions; regulatory reporting requirements for individual cases and aggregate data safety reports such as DSURs and PBRERs in the pre- and post-marketing phases respectively.

11.6. Predisposing factors and the impact of pre-existing disease and intrinsic/extrinsic factors on the susceptibility for, and severity of adverse events, and how to minimise this impact.

11.7. Post-marketing safety assessment and reporting; sources of safety data including spontaneous reporting, medical / scientific literature, media, social media reports; post authorisation efficacy and safety studies, real-world evidence studies, non-interventional studies, drug utilisation studies. Prescription event monitoring (PEM), patient registries, digital sources such as health authority and pharma company adverse event databases and methods of evaluation such as Bayesian analysis and proportionate hazards model.

11.8. Reportable events: overdose, medication errors, off-label use, misuse and abuse, lack of efficacy, experience during pregnancy and breast feeding.

11.9. Drug interactions and impact on benefit-risk including impact of factors such as pharmacogenomic aspects.

11.10 Pharmacoepidemiological approaches for pharmacovigilance; sources of information, study designs and data analysis; monitoring of risk mitigation activities.

11.11. Safety signal management pre- and post-marketing, including detection and validation of signals, evaluation and categorisation of risks.

11.12. Pre- and post-authorisation risk mitigation and management including issue and crisis management.

11.13. Risk communication to investigators, prescribers, regulatory authorities and patients; passive e.g. labelling changes vs active approaches e.g. direct healthcare professional communication (DHPC), controlled supply to validated sites, prescriber training.

Section 12. Medicines Information, Education, Promotion: Communication Strategies and Channels.

12.1. Relevant codes of conduct, policy, procedures and regulations for pre-approval and post-approval activities including Good Promotional Practice.

12.2. Non-promotional & scientific communications across a medicine's lifecycle, disease awareness, medical information and education.

12.3. Publication strategy for clinical trials and clinical research studies: guidelines for selection of journals and good writing practices; guidelines for quality of production. Lay language summaries.

12.4. Support of the development of clinical practice guidelines, and then dissemination.

12.5. Interactions with patients, caregivers and patient organisations: ethics and compliance, communication and disclosures; governance of interactions.

12.6. Non-promotional product support: medical information, direct healthcare professional communication (DHPC) and other non-promotional activities, pre & post-licence activities.

12.7. Principles and practice of marketing: market structure and competition, market analysis & market research, strategy, communication and tactics.

12.8. Advertising: claims, prescribing information, media and digital methods, target audiences, compliance, ethics, principles of oversight and approval.

12.9. Educating stakeholders: principles of continuing professional education, designing patient & public education.

Section 13. Health Economics, Outcomes Research, Pharmacoeconomics and Patient Access

13.1. Introduction to corporate social responsibility and managerial economics: equitable access to healthcare, ecological sustainability, financial statements, forecasting.

13.2. International public health policies, health systems performance, essential medicines, universal health coverage.

13.3 Healthcare systems typology, public and private health insurance models; flow of funds.

13.4 Principles and methods for health economics (macro and micro) and outcomes research; pharmacoeconomic concepts and the role of patients.

13.5 Evidence-based medicine: clinical and pharmacoeconomic evidence, clinician-related, patient-related.

13.6. Health technology assessment and market access at the international, national and local levels. Consideration for advanced therapeutic medicinal products. Budget impact analysis, pricing strategy.

13.7. The qualitative and quantitative appraisal of health-economic evidence, systematic reviews and meta-analyses pre- and post-approval.

13.8. Health-related quality of life, patient-reported outcome measures, patient-reported experience measures; preference studies using discrete choice experiment (DCE) methodology.

13.9. Commercial strategies and lifecycle management: competition, licensing, intellectual property, co-marketing and repositioning, generics, biosimilars, parallel imports and switching strategies.

13.10. Patient accessibility to medicines: compassionate use, patient access schemes, individual finance requests by hospitals, clinicians, charities, patient organisations, non-governmental organisations.