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Appendix 12.5 to
PharmaTrain Manual

MRA
MASTER OF
REGULATORY
AFFAIRS

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This PharmaTrain programme in medicines regulatory affairs in Europe is jointly offered by the Universities of Basel, Copenhagen, Hertfordshire and King's College, London.

The programme was jointly developed by the universities, EFPIA partners in PharmaTrain as well as competent authorities in Europe

The "Master of Regulatory Affairs" (MRA) Programme is offered to postgraduate students wishing to obtain a MSc

PharmaTrain
MASTERING MEDICINES DEVELOPMENT

We are an official partner of the European IMI PharmaTrain project and adapt our training activity to the new shared standards of PharmaTrain. PharmaTrain is one of the IMI JU projects on Education and Training and addresses Pharmaceutical Medicine/Drug Development Sciences. IMI stands for Innovative Medicines Initiative, a Joint Undertaking of the European Commission and European Federation of Pharmaceutical Industries and Associations, EFPIA.
Consult www.imi.europa.eu and www.pharmatrain.eu

PharmaTrain
MASTERING MEDICINES DEVELOPMENT

Key words:

- Universities Basel, Copenhagen, Hertfordshire, and King's College, London
- Post-graduate Master of Regulatory Affairs
- Regulatory affairs
- Medicinal products / Pharmaceuticals
- IMI PharmaTrain project
- Joint undertaking EC and EFPIA
- Integrated product development
- Market introduction
- Life Cycle Management

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The Master of Regulatory Affairs Programme

A new programme leading to the degree “Master of Regulatory Affairs” (MRA) will be offered jointly by the Universities of Basel, Copenhagen, Hertfordshire and King’s College, London. It provides a systematic and comprehensive immersion in modern medicinal product regulation, and regulatory aspects of integrated product development and market introduction. It is designed primarily to meet the needs of professionals working for government regulatory agencies and other decision- and policy-making bodies, the life science industries, including the service industry, and the academic environment.

The Master of Regulatory Affairs programme covers all aspects of the regulatory requirements of drug development, organized into mandatory modules, comprising:

- Medicines development and regulation
- EU Regulation and Legislation
- EU/EEA Regulatory Procedures and Requirements
- Pharmaceutical Development and Quality
- Non-clinical Development
- Clinical Development
- Pharmacovigilance: from Classic Pharmacovigilance to Managing Benefit-Risk
- Regulatory Strategic Planning prior to initial Marketing Authorization Applications
- Regulatory Strategic Planning and Life Cycle Management after initial Marketing Authorization
- Quality Management and Inspections.

In addition, (two) elective modules are to be chosen from (additional) regulatory affairs topics, the broader PharmaTrain Continuing Professional Development (CPD) platform, as well as from other partner courses (see also OnCourse).

Participation in the MRA programme will not only provide opportunities to integrate work and education and gain in-depth knowledge of the subject matter but will also support interactions with experts – face-to-face or online – and development of an international contact network.

Opportunities to attend single Modules of the MRA Programme will be made available on an ad hoc basis pending availability of seats.

The teaching faculty will comprise experts of international repute from competent authorities, academia and industry.

We look forward to working with you on behalf of PharmaTrain

University of Basel	*University of Copenhagen*	*King’s College, London*	*Univ. Hertfordshire, Hatfield*
Dr. Annette Mollet	Anne Marie Shuhaiber Clemensen	Prof. Brian Gennery	*Matt Traynor*

Glossary

Vision

The vision of the MRA programme is to provide a comprehensive postgraduate education in medicines regulatory affairs in Europe. This will support to optimize development of better medicines to better serve the needs of patients and public health. The goal is to enhance the regulatory expertise, knowledge and skills required to ensure a competitive and sustainable European pharmaceutical sector in modern medicines discovery, development, pre-authorization, authorization and post-authorization.

Objectives

To provide a comprehensive knowledge and understanding of the regulatory rules and requirements applicable to medicines development and lifecycle management, and the competence to apply them to:

- the medicines development process
- the strategic planning and application of the regulatory requirements throughout the lifecycle of a medicine
- the ongoing evaluation of benefit-risk throughout the lifecycle of a medicine
- quality management
- good regulatory practices

Who should attend?

The MRA is a postgraduate training programme designed for professionals working in government regulatory agencies, the life science industry and universities, who wish to acquire or expand knowledge and expertise in regulatory aspects of medicines development. Applicants are normally expected to have a life science degree and at least 2 years' relevant working experience.

About the Course

Curriculum

The MRA curriculum is designed in accordance with the European Bologna agreements on mutual recognition amongst participating universities. Coursework is achieved by a combination of face-to-face participation, homework, blended and e-learning, including assignments for each module.

Awarding of an MRA is contingent upon achievement of 60 European Credit Points (ECTS) from compulsory and elective modules, and completion of an MSc thesis (see below). Successful completion of individual modules can also be certified on a module-by-module basis.

Work-based experience can be added to foster competence.

Whilst the usual time-frame for completing the modules of the Masters programme is expected to be two to four years, requests for extensions can be addressed on a case-by-case basis to the enrolling university.

Mandatory and Elective Modules

The mandatory introductory module (Module 1) provides a complete overview of medicines development. For those wishing to complete the full programme, this is the prerequisite for completion of other compulsory modules. It focuses on the pharmaceutical development

process across the entire life cycle of a medicinal product to provide a context for the subsequent in-depth study of regulatory affairs.

Mandatory Modules 2-10 encompass all areas of regulatory affairs as applied to scientific development of pharmaceuticals before and after marketing authorisation. They also address new and advanced therapies and products, as well as special or vulnerable patient populations such as children of various age groups, and treatments for orphan diseases.

For the Elective Modules (11-12), the topic(s) can be chosen from a variety of themes. Options may include other regulatory topics and/or other topics such as those offered by the PharmaTrain CPD platform (see also www.pharmatrain.eu), and related courses.

Each Module will include assignments to be completed in the student's own time (including by e-learning).

Masters Thesis
To fulfil the university requirements for obtaining an MSc it is necessary to submit and defend a thesis. The theme of the Masters thesis should be chosen early, in agreement with the supervisor at the enrolling university.

Four Collaborating Universities

The modular structure adopted by all universities will make it possible for students to complete individual modules at the university of their choice, taking into account national peculiarities to be re-calculated into ECTS.

The Universities' Governance set out in a Memorandum of Understanding (MoU) provides all details of relevance for students.

For the time being, a joint degree is not offered.

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Course Objectives (using the Bologna credit system, where each Module is accredited with 5 ECTS)

To provide regulatory, industry, and university professionals with a comprehensive understanding of the regulatory rules and requirements as applied to medicines development and lifecycle management, along with the competence to apply them to:

- the medicines development process
- strategic planning and the application of the regulatory requirements throughout the lifecycle of a medicine
- the ongoing evaluation of benefit-risk throughout the lifecycle of a medicine
- quality management
- good regulatory practices

Course Learning Objectives

After successful completion of the 10 compulsory modules of this course, the student should be able to apply Good Regulatory Practices in support of the following:

1. Understand and apply the general principles of medicines development and regulation
2. Critically discuss and appraise currently available and upcoming legislation in the EU
3. Understand, organize and prepare the various types of regulatory procedures during medicines development and appreciate the impact on marketing authorisation issues and documentation
4. Determine and manage the generation and provision of quality data and documentation for pharmaceutical development throughout the lifecycle of a product
5. Recognise, distinguish and manage non-clinical development/data for medicines development and its reflection in product information and/or the safety risk management plan of a product
6. Appraise, interpret and apply clinical trials legislation and related guidelines to the design and implementation of clinical trial programmes, as well as translation of clinical trial data into regulatory submission dossiers and product information
7. Understand and explain the roles and the impact of pharmacovigilance and the risk management plan on the use of medicines before and after marketing authorisation, and their implications for public health
8. Identify, select and apply the regulatory and business considerations that drive decision-making throughout the development lifecycle before and after marketing authorisation as they apply to specific product types
9. Plan for, prepare and implement the necessary regulatory procedures for the continuous product development during the lifecycle of the medicine, before and after marketing authorization
10. Discuss, interpret and apply the principles and key elements of a quality management system and understand its role in ensuring compliance with GxP

List of Regulatory Affairs' Topics (Modules for the ECTS system):

– Mandatory Topics
  - Introductory Module: The Principles of Medicines Development and Regulation
  - EU Regulation & Legislation
  - Regulatory Procedures and Requirements in the European Union/EEA
  - Pharmaceutical Development and Quality
  - Non-clinical Development
  - Clinical Development
  - Pharmacovigilance: from Classic Pharmacovigilance to Managing Benefit-Risk
  - Regulatory Strategic Planning prior to Initial Marketing Authorisation
  - Regulatory Strategic Planning and Life Cycle Management after Initial Marketing Authorisation
  - Quality Management and Inspections

  - Elective Topics:
  - The four universities have agreed to develop and present a number of elective modules, such as:
    - International Regulatory Affairs
    - Quality: Biological Products, Biotechnology and Advanced Therapy Medicines
    - Medical Devices and Combination Products, "Borderline Products", Novel Foods
    - etc.
  - Other topics are recommended as useful to some regulator, and are available within PharmaTrain or via the On-Course Platform, such as:
    - Ethics
    - Managing international and national Health Care Compliance requirements

See: www.pharmatrain.eu . See also PharmaTrain Manual

Module 1: Introductory Module: The Principles of Medicines Development and Regulation

LEARNING AIMS
1. Understand what a Medicinal Product is and how it is defined in terms of Quality, Safety and Efficacy during the development and throughout the medicinal product's lifecycle
2. Understand the importance of Benefit – Risk assessment during development and throughout a medicinal products lifecycle
3. Describe the interrelationships between regulatory bodies and pharmaceutical industry during a medicinal product's lifecycle

LEARNING OUTCOMES
After successful completion of this module, the student should be able to:
1. Categorise the steps in the overall medicines development process from discovery to approval, patient access and during the post-approval phase
2. Discuss the need for, and describe the types of, ongoing benefit-risk management and optimization throughout the lifecycle of a medicinal product
3. Categorise and appraise the general principles of medicines regulation (both pre- and post-approval) at EU and global level
4. Organise and explain the regulatory aspects of drug development in terms of quality, non-clinical and clinical testing
5. Identify interaction points with quality, non-clinical and clinical disciplines during medicines development
6. Appraise the role of quality management systems in the medicines development process
7. Delineate the roles and responsibilities of Regulatory Affairs personnel during the medicines development process and during lifecycle management

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOMES
1.1	**The global pharmaceutical development process from discovery to marketing and maintenance (lifecycle management)** • Definition of a medicinal product • Target Product Profile (TPP) • Development plans • Project milestones • Critical factors and bottlenecks • Role of key players during drug development and post-approval	1. Categorise the steps in the overall medicines development process from discovery to approval, patient access and during the post-approval phase 2. Discuss the need for, and describe the types of, ongoing benefit-risk management and optimization throughout the lifecycle of a medicinal product 5. Identify interaction points with quality, non-clinical and clinical disciplines during medicines development 7. Delineate the roles and responsibilities of Regulatory Affairs personnel during the medicines development process and during lifecycle management
1.2	**European and global regulatory principles** • Rules, Regulations and restraints • The regulatory framework in EU and US • International Conference of Harmonisation (ICH) and other guidance documents • European Medicines Agencies (EMA) and National Competent Authorities (NCA) • Regulatory strategic considerations • Regulatory procedures • Common Technical Documents (CTD), Summary of Product Characteristics (SmPC), Package Leaflet (PL) and labelling • Information to the public and legal aspects of marketing	2 Discuss the need for, and describe the types of, ongoing benefit-risk management and optimization throughout the lifecycle of a medicinal product 3. Categorise and appraise the general principles of medicines regulation (both pre- and post-approval) at EU and global level 5. Identify interaction points with quality, non-clinical and clinical disciplines during medicines development 7. Delineate the roles and responsibilities of Regulatory Affairs personnel during the medicines development process and during lifecycle management
1.3	**Basic principles of Quality Management / Quality Control / Quality Assurance** • Basic principles of GxP • Quality risk management, Audits and Inspections	6. Appraise the role of quality management systems in the medicines development process

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOMES
1.4	**Basic principles of pharmaceutical quality** • Development of drug substance and drug product • Requirements and critical issues incl. GMP • The ICH vision – Q8, Q9, Q10 and Q11 • CMC documentation in relation to the clinical phases • Interface with non-clinical safety and clinical research • Product development and post-approval maintenance	2. Discuss the need for, and describe the types of, ongoing benefit - risk management and optimization throughout the lifecycle of a medicinal product 3. Categorise and appraise the general principles of medicines regulation (both pre- and post-approval) at EU and global level 5. Identify interaction points with quality, non-clinical and clinical disciplines during medicines development 7. Delineate the roles and responsibilities of Regulatory Affairs personnel during the medicines development process and during lifecycle management
1.5	**Basic principles of non-clinical development** • Introduction to medicinal chemistry, pharmacology, pharmacokinetics and toxicology • Setting the scene for entering into man • Interface with quality development and clinical research • Decision points for entering - and continuation of clinical development in relation to safety & efficacy • Contribution to Risk assessment (including environmental) • Good Laboratory Practice (GLP)	2. Discuss the need for, and describe the types of, ongoing benefit - risk management and optimization throughout the lifecycle of a medicinal product 3. Categorise and appraise the general principles of medicines regulation (both pre- and post-approval) at EU and global level 4. Organise and explain the regulatory aspects of drug development in terms of quality, non-clinical and clinical testing 5. Identify interaction points with quality, non-clinical and clinical disciplines during medicines development 7. Delineate the roles and responsibilities of Regulatory Affairs personnel during the medicines development process and during lifecycle management
1.6	**Basic principles of clinical efficacy and safety** • Clinical pharmacology • Exploratory vs. confirmatory studies • Defining the use of the product • Observational studies • Statistics and data management • Benefit/risk assessment including Good Clinical Practice (GCP)	2. Discuss the need for, and describe the types of, ongoing benefit - risk management and optimization throughout the lifecycle of a medicinal product 3. Categorise and appraise the general principles of medicines regulation (both pre- and post-approval) at EU and global level 4. Organise and explain the regulatory aspects of drug development in terms of quality, non-clinical and clinical testing

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOMES
		5. Identify interaction points with quality, non-clinical and clinical disciplines during medicines development 7. Delineate the roles and responsibilities of Regulatory Affairs personnel during the medicines development process and during lifecycle management
1.7	**European regulatory safety activities, pharmacovigilance activities and life cycle management in general** • Pharmacovigilance activities • Prediction and management of safety risks throughout product lifecycle, i.e. before and after marketing authorization (MA) • Lifecycle management • New formulations • Marketing and legal aspects • Public health risk	1. Categorise the steps in the overall medicines development process from discovery to approval, patient access and during the post-approval phase 2. Discuss the need for, and describe the types of, ongoing benefit-risk management and optimization throughout the lifecycle of a medicinal product 3. Categorise and appraise the general principles of medicines regulation (both pre- and post-approval) at EU and global level 5. Identify interaction points with quality, non-clinical and clinical disciplines during medicines development 7. Delineate the roles and responsibilities of Regulatory Affairs personnel during the medicines development process and during lifecycle management
1.8	**Roles and responsibilities of Regulatory Affairs personnel** • The history and role of Regulatory Affairs • The diversity in roles and responsibilities within Regulatory Affairs in headquarters, an affiliate and a small biotech company • How to work with Good Regulatory Practices • Development of Regulatory Affairs personnel in line with current legislation and guidelines and anticipation of future trends • Assure cross-functional compliance with regulatory requirements	2. Discuss the need for, and describe the types of, ongoing benefit-risk management and optimization throughout the lifecycle of a medicinal product 3. Categorise and appraise the general principles of medicines regulation (both pre- and post-approval) at EU and global level 4. Organise and explain the regulatory aspects of drug development in terms of quality, non-clinical and clinical testing 5. Identify interaction points with quality, non-clinical and clinical disciplines during medicines development 7. Delineate the roles and responsibilities of Regulatory Affairs personnel during the medicines development process and during lifecycle management

Module 2: EU Regulation & Legislation

***Module 2 Key messages**:*

- To note similarity of regulatory principles in different jurisdictions, with differences in implementation and assessment approaches
- To appreciate different implementation of Directives in different EU Member States
- To appreciate medicines regulation as a means to improve (optimise) public health

LEARNING AIMS
1. Understand the principles of the EU legal system for medicinal products and the collaboration with Institutions outside the EU
2. Understand how the position in a product's patent / data exclusivity cycle determines the type of application that is possible and/or required and the marketing options available (e.g. line extensions; generics; legal reclassification)
3. Understand how the legislation and guidance documents help establish benefit *versus* risk
4. Appreciate the dynamic nature of the regulatory legislative context which continuously evolves in keeping with societal changes
5. For each medicine to understand current mechanisms for anticipating and addressing unknown characteristics (e.g. PIPs and RMPs; Guideline development, legislative changes);
6. Understand the different purposes of Summary of Product Characteristics, Package Leaflets, and labels

LEARNING OUTCOMES
After successful completion of this module, the student should be able to:
1. Discuss and distinguish the principles of EU and National legislative provisions as applied to medicinal products
2. Compare and evaluate the roles and responsibilities of key players in the EU regulatory process
3. Critically discuss challenges of introducing and implementing new legislation
4. Discuss and appraise the key legislation underpinning each step of medicines development and life-cycle management
5. Describe the co-operation with other regulatory stakeholders
6. Discuss how the Summary of Product Characteristics and Package Leaflets develop over time

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
2.1	**Introduction to Regulatory Affairs** • History and development of the regulatory framework (EU, US and Japan) and its role in public health • Introduction to International Conference on Harmonisation (ICH) • Introduction to the Common Technical Document (CTD) structure	1. Discuss and distinguish the principles of EU and National legislative provisions as applied to medicinal products 2. Compare and evaluate the roles and responsibilities of key players in the EU regulatory process 3. Critically discuss challenges of introducing and implementing new legislation 5. Describe the co-operation with other regulatory stakeholders
2.2	**EU pharmaceutical legislation (see also elective modules for other regions)** • The regulatory framework • Regulations and Directives • Guidance documents including Notice to Applicants, Commission Communications; Administrative guidance and Scientific guidelines • Special populations and incentives (e.g. paediatrics, orphan drugs and other special populations), compassionate use • Accommodating new legislation • Introduction to related legislation (data exclusivity; patent law; civil law etc.)	1. Discuss and distinguish the principles of EU and National legislative provisions as applied to medicinal products 2. Compare and evaluate the roles and responsibilities of key players in the EU regulatory process 3. Critically discuss challenges of introducing and implementing new legislation 4. Discuss and appraise the key legislation underpinning each step of medicines development and life-cycle management
2.3	**EU infrastructure** • European Commission • The European medicines regulatory network: National Competent Authorities (NCAs), Heads of Medicines Agencies (HMA), European Medicines Agency (EMA) (incl. Committees and Working Parties) • National Competent Authorities • Electronic systems for data sharing (EudraCT, EudraVigilance et) • Links with other (non-EU) regions (e.g. US and Japan)	1. Discuss and distinguish the principles of EU and National legislative provisions as applied to medicinal products 2. Compare and evaluate the roles and responsibilities of key players in the EU regulatory process 3. Critically discuss challenges of introducing and implementing new legislation 5. Describe the co-operation with other regulatory stakeholders
2.4	**Marketing Authorisation dossiers** • CTD (paper/electronic format and content) • Summary of product Characteristics (SmPC), Package Leaflet (PL), label (packaging) • Liability and Labelling • Support provided by IT and templates (e.g. eCTD/NeeS, Quality Review of Documents (QRD),and summary tables)	2. Compare and evaluate the roles and responsibilities of key in the EU regulatory process 3. Critically discuss challenges of introducing and implementing new legislation 6. Discuss how Summary of Product Characteristics and Package Leaflets develop over time

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	**LEARNING OUTCOME(S)**
2.5	**Principles of EU regulatory procedures** • Scientific Advice and Protocol Assistance • Clinical Trial Application (CTA) and ethical review • Orphan Drugs • Paediatric Investigation Plan (PIP) • Environmental risk assessment • Procedures for Marketing Authorisations • Patents l and data exclusivity • Types of applications (Full / Stand alone; Generic; Abridged, Hybrid etc.) • Referrals • Pharmacovigilance including Risk Management Plans • Renewals and the sunset clause • Variations	1. Discuss and distinguish the principles of EU and National legislative provisions as applied to medicinal products 2. Compare and evaluate the roles and responsibilities of key players in the EU regulatory process 4. Discuss and appraise the key legislation underpinning each step of medicines development and life-cycle management 5. Describe the co-operation with other regulatory stakeholders 6. Discuss how Summary of Product Characteristics and Package Leaflets develop over time
2.6.	**Falsified medicines and illegal supply of medicines** REVISIT PLACEMENT • Implications of EU Falsified Medicines Directive and Medicrime Convention of Council of Europe • Supply chain integrity	1. Discuss and distinguish the principles of EU and National legislative provisions as applied to medicinal products 4. Discuss and appraise the key legislation as applied to medicinal products underpinning each step of medicines development and life-cycle management

Module 3: Regulatory Procedures and Requirements in the European Union/EEA

***Module 3 Key messages**:*

- To note that there are multiple routes of entry onto the EU market, but once granted, all Marketing Authorizations obey the same rules for lifecycle management [covered in more detail in Module 9]

LEARNING AIMS	
1.	Understand the type of application/procedure needed and its challenges, opportunities and regulatory requirements at each stage of a product's development / lifecycle
2.	Understand the workflow underlying data capture and document management and how these affect how the dossier is compiled
3.	Understand how compiling the dossier affects the timing of submissions including readability testing and translations
4.	Understand the challenges and opportunities of specific legislation (e.g. paediatric regulation, orphan medicines regulation, advanced therapies)

LEARNING OUTCOMES	
After successful completion of this module, the student should be able to:	
1.	Appraise the requirements for different types of scientific advice, and application procedures according to the medicinal product/context in the EU/EEA
2.	Determine and propose the most appropriate procedural route according to medicinal product/context in the EU/EEA
3.	Determine and plan when, why, how and where to seek scientific advice
4.	Understand, organise and prepare the regulatory procedures for special populations (including paediatric use, orphan diseases and other special groups)
5.	Propose and develop product information documents
6.	Understand the workflow underlying data capture and document management and how these affect dossier compilation
7.	Assess and discuss the key elements for the maintenance of a Marketing Authorization including legal status and principles of changes in classification

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
3.1	**Scientific Advice** • Why, when, how and where to apply for scientific advice • National vs. CHMP advice, pros and cons • Protocol assistance • Pre-submission meetings • EMA/FDA joint scientific advice • EMA/Member State Business Pipeline meetings	1. Appraise the requirements for the different types of scientific advice and application procedures according to the medicinal product/context in the EU/EEA 3. Determine and plan when, why, how and where to seek scientific advice
3.2	**Clinical Trial Applications** • EudraCT and other clinical trial registries • IMPD guideline • Timelines and submission to regulatory authorities and ethics committees • Substantial amendments; Annual Safety Report; End of Trial Notification	1. Appraise the requirements for the different types of scientific advice and application procedures according to the medicinal product/context in the EU/EEA 3 Determine and plan when, why, how and where to seek scientific advice 6. Understand the workflow underlying data capture and document management and how these affect dossier compilation
3.3	**Orphan Medicinal Products** • Legal basis • Small population guideline • Procedure for obtaining designation • Timelines and fees • Role of Committee for Orphan Medicinal Products (COMP) • Opportunities (market exclusivity) and limitations	4. Understand, organise and prepare the regulatory procedures for special populations (including paediatric use, orphan diseases and other special groups) 5. Propose and develop product information documents
3.4	**Medicinal products for paediatric use** • Paediatric Investigation Plan (PIP) • Procedures (incl. format and content of applications) • Role of Paediatric Committee (PDCO) • Paediatric Use Marketing Authorisation (PUMA) • Medicinal Products for Paediatric Use (ref to Articles 45/46) • Challenges and opportunities of paediatric regulation	4. Understand, organise and prepare the regulatory procedures for special populations (including paediatric use, orphan diseases and other special groups) 5. Propose and develop product information documents
3.5	**Electronic submissions** • eCTD vs NeeS (version control, naming, maintain an audit trail) • e-application forms (eAF) • Challenges and opportunities, (interfaces, compatibility etc.)	6. Understand the workflow underlying data capture and document management and how these affect dossier compilation

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
3.6	**Development of Product Information – from data to SmPC** • SmPC's, PL's, Labelling • Translation • Readability testing of PLs • Labels • Labelling requirements & compliance (Braille, etc.)	5. Propose and develop product information documents 7. Assess and discuss the key elements for the maintenance of a Marketing Authorization including legal status and principles of changes in classification
3.7	**Applications for Marketing Authorisations for Medicinal Products** • Content and format of MAA • Data requirements for special populations • MA in relation to protection of industrial and commercial (intellectual) properties: Data exclusivity, marketing & patent protection • MA in relation to special considerations (fixed combination products; drug-device combinations) Content and format • Pharmacovigilance requirements	1. Appraise the requirements for the different types of scientific advice and application procedures according to the medicinal product/context in the EU/EEA 2. Determine and propose the most appropriate procedural route according to medicinal product / context in the EU/EEA including maintenance 4. Understand, organise and prepare the regulatory procedures for special populations (including paediatric use, orphan diseases and other special groups) 5. Propose and develop product information documents 6. Understand the workflow underlying data capture and document management and how these affect dossier compilation
3.8	**Marketing Authorisations of generic and biosimilar medicinal products** • Data exclusivity • Content and format of MAA • Well-established medicinal use	1. Appraise the requirements for the different types of scientific advice and application procedure according to the medicinal product/context in the EU/EEA 2. Determine and propose the most appropriate procedural route according to medicinal product/context in the EU/EEA 5. Propose and develop product information documents 6. Understand the workflow underlying data capture and document management and how these affect dossier compilation
3.9	**Herbal and complementary medicines:** • Herbal and homoeopathic: authorisation vs. registration • Traditional Chinese Medicine (TCM) • Ayurvedic medicines	1. Appraise the requirements for the different types of scientific advice and application procedures according to the medicinal product/context in the EU/EEA

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
		5. Propose and develop product information documents 6. Understand the workflow underlying data capture and document management and how these affect dossier compilation
3.10	**The Centralised Procedure** • Centralised Procedure (legal basis, role of EMA, eligibility, pre-submission dialogue, procedure for filing application, fees, selection of rapporteurs, timelines, operational aspects, pros/cons, appeal procedure) • Accelerated procedure, conditional approval, exceptional circumstances • Transparency • Post-approval obligations • Annual reports • EU/US – differences and similarities	1. Appraise the requirements for the different types of scientific advice and application procedures according to the medicinal product/context in the EU/EEA 2. Determine and propose the most appropriate procedural route according to medicinal product/context in the EU/EEA 4. Understand, organize and prepare the regulatory procedures for special populations (including paediatric use, orphan diseases and other special groups) 5. Propose and develop product information documents
3.11	**National Procedures** • Legal basis, -Filing the application; fees; timelines; granting of national authorisations; operational aspects • Types of products • Transparency (Agencies' websites, press releases, Public assessment reports, etc.)	1. Appraise the requirements for the different types of scientific advice, Clinical Trial Applications, and Marketing Authorization Application procedure according to the medicinal product/context in the EU/EEA 2. Determine and propose the most appropriate procedural route according to medicinal product/context in the EU/EEA 5. Propose and develop product information documents

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
3.12	**The Mutual Recognition & Decentralised Procedures** • Legal basis, Selection and role of RMS, obligations of CMS • Filing the application; fees; timelines; granting of national authorisations; operational aspects • Types of products • Referrals • Transparency (Public assessment reports etc.) • Role of the Coordination Group for Mutual Recognition and Decentralised Procedure (CMDh)	1. Appraise the requirements for the different types of scientific advice and application procedures according to the medicinal product/context in the EU/EEA 2. Determine and propose the most appropriate procedural route according to medicinal product / context in the EU/EEA 5. Propose and develop product information documents
3.13	**Line Extension and Variation Applications** • Legal basis, types of application • Content and format • Variations regulation (scope and status) • Downgrading, grouping and consequential changes	1. Appraise the requirements for the different types of scientific advice and application procedures according to the medicinal product/context in the EU/EEA 2. Determine and propose the most appropriate procedural route according to medicinal product / context in the EU/EEA 5. Propose and develop product information documents 7. Assess and discuss the key elements for the maintenance of a Marketing Authorization, including legal status and principles of changes in classification
3.14	**Legal status and reclassifications, renewal and deregistration** • Legal basis • Sunset clause	1. Appraise the requirements for the different types of scientific advice and application procedures according to the medicinal product/context in the EU/EEA 5. Propose and develop product information documents 7. Assess and discuss the key elements for the maintenance of a Marketing Authorization, including legal status and principles of changes in classification

Module 4: Pharmaceutical Development and Quality

***Module 4 Key messages**:*

- Appreciate the need for a change management process and for traceability
- Appreciate the need to provide up-to-date amounts of quality documentation for non-clinical investigations, clinical investigations and post-approval activities

LEARNING AIMS	
1.	Understand which documents are required for the quality dossier and the need for inclusion of documents to ensure traceability of product constituents.
2.	Understand the need for equivalence of product from clinical trials to currently marketed product and how finished Product Specification and validation ensure this
3.	Appreciate how product usage may affect stability, storage, packaging and labeling requirements
4.	Appreciate the need for a change management process; appreciate the timelines for generating new data to meet new manufacturing or packaging requirements
5.	Understand how to deal with deviations from specification and changes in the quality dossier
6.	Understand that EDQM assessment is conducted to the same standard as for an individual product and when use of a Certificate of Suitability is appropriate

LEARNING OUTCOMES	
After successful completion of this module, the student should be able to:	
1.	Explain the concept and importance of GMP for the manufacture of medicines in the pre- and post-approval phases
2.	Appraise the regulatory and business considerations in pharmaceutical development
3.	Discuss the quality data requirements for the active substance and the medicinal product
4.	Critically review the processes for ensuring the equivalence of a marketed product with formulations used for non-clinical and clinical development
5.	Discuss and propose the regulatory management of pharmaceutical quality data pre- and post-approval
6.	Determine and manage how the pharmaceutical quality data are reflected in the product information
7.	Predict, revise and evaluate the potential requirement for additional pharmaceutical quality data during the life-cycle of a medicinal product

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
4.1	**Development of drug substance and drug product - place in the overall development programme** • Perspectives on CMC (Chemistry, Manufacturing and Controls) Drug Development from pre-development to commercialisation • Interfaces and collaboration with other disciplines • Supporting activities in Drug Development	2. Appraise the regulatory and business considerations in pharmaceutical development 3. Discuss the quality data requirements for the active substance and the medicinal product 4. Critically review the processes for ensuring the equivalence of a marketed product with formulations used for non-clinical and clinical development 6. Determine and manage how the pharmaceutical quality data are reflected in the product information
4.2	**Regulatory requirements for CMC development** • Rationale and introduction to GMP • Relevant guidelines including ICH guidelines • Quality by design	1. Explain the concept and importance of GMP for the manufacture of medicines in the pre- and post-approval phases 3. Discuss the quality data requirements for the active substance and the medicinal product 4. Critically review the processes for ensuring the equivalence of a marketed product with formulations used for non-clinical and clinical development 5. Discuss and propose the regulatory management of pharmaceutical quality data pre- and post-approval
4.3	**Drug substance synthesis and characterisation** • Manufacturing process, Starting materials, Process controls, Material controls • Critical steps and Process validation • Elucidation of structure • Physico-chemical characterisation	3. Discuss the quality data requirements for the active substance and the medicinal product 5. Discuss and propose the regulatory management of pharmaceutical quality data pre- and post-approval 6. Determine and manage how the pharmaceutical quality data are reflected in the product information

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
4.4	**CMC documentation in relation to clinical development phases** • Background and guidelines • Interface between CMC development and non-clinical and clinical data • Critical issues and requirements for CMC documentation that supports different clinical development phases • IMPD requirements in different phases of development	1. Explain the concept and importance of GMP for the manufacture of medicines in the pre- and post-approval phases 2. Appraise the regulatory and business considerations in pharmaceutical development 3. Discuss the quality data requirements for the active substance and the medicinal product 4. Critically review the processes for ensuring the equivalence of a marketed product with formulations used for non-clinical and clinical development 6. Determine and manage how the pharmaceutical quality data are reflected in the product information
4.5	**Drug Product** • Pharmaceutical development • Manufacturing process • Process controls, validation and critical steps	1. Explain the concept and importance of GMP for the manufacture of medicines in the pre- and post-approval phases 2. Appraise the regulatory and business considerations in pharmaceutical development 3. Discuss the quality data requirements for the active substance and the medicinal product 4. Critically review the processes for ensuring the equivalence of a marketed product with formulations used for non-clinical and clinical development 5. Discuss and propose the regulatory management of pharmaceutical quality data pre- and post-approval

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
4.6	**Control of drug substance and drug product** • Analytical procedures • Validation – Methodology • Batch analysis • Specifications during development • Final specification and justification of specification • Impurities including Residual Solvents, Heavy metal catalysts and Genotoxic impurities • Pharmacopoeial perspectives	1. Explain the concept and importance of GMP for the manufacture of medicines in the pre- and post-approval phases 3. Discuss the quality data requirements for the active substance and the medicinal product 4. Critically review the processes for ensuring the equivalence of a marketed product with formulations used for non-clinical and clinical development 5. Discuss and propose the regulatory management of pharmaceutical quality data pre- and post-approval 6. Determine and manage how the pharmaceutical quality data are reflected in the product information
4.7	**Stability, drug substance and drug product** • Stability programs • Matrixing and bracketing • Climatic zones – specific requirements for different geographic regions • Container closure systems • Post-approval commitments	1. Explain the concept and importance of GMP for the manufacture of medicines in the pre- and post-approval phases 3. Discuss the quality data requirements for the active substance and the medicinal product 5. Discuss and propose the regulatory management of pharmaceutical quality data pre- and post-approval 6. Determine and manage how the pharmaceutical quality data are reflected in the product information 7. Predict, revise and evaluate the potential requirement for additional pharmaceutical quality data during the life-cycle of a medicinal product
4.8	**The Quality Overall Summary - CTD** • Objectives of Quality Overall Summary • Tabulations / graphical presentations • Critical Quality Issues • Regional information	1. Explain the concept and importance of GMP for the manufacture of medicines in the pre- and post-approval phases 2. Appraise the regulatory and business considerations in pharmaceutical development 3. Discuss the quality data requirements for the active substance and the medicinal product 6. Determine and manage how the pharmaceutical quality data are reflected in the product information

Module 5: Non-clinical Development

Module 5 Key messages:

- Non-clinical information provides an essential contribution to development throughout the lifecycle of a medicinal product

LEARNING AIMS:	
1.	Understand what non-clinical data are required for CTAs at different stages of development
2.	Understand what type of studies are required to support the intended use of a given medicinal product
3.	Appreciate the need to address relevant non-clinical issues in the clinical part of the MAA dossier
4.	Understand when and why an environmental risk assessment is needed
5.	Understand what additional requirements may apply when non-standard assays and species are used
6.	Understand how the results from non-clinical studies are to be summarised in the product information and the Risk Management Plan
7.	Appreciate that the need for different types of studies may evolve during the medicinal product's lifecycle.

LEARNING OUTCOMES
After successful completion of this module, the student should be able to:
1. Recognise, distinguish and propose the type of non-clinical development / study requirements according to the proposed use of the medicinal substance (both chemical and biological substances)
2. Recognise, distinguish and propose the type of non-clinical studies required at different stages of development
3. Appreciate when an environmental risk assessment is required
4. Evaluate and manage how the non-clinical issues are addressed in the regulatory submission dossiers
5. Determine and manage how the non-clinical study findings are reflected in the product information and the Risk Management Plan
6. Predict, revise and evaluate the potential requirement for additional non-clinical studies during the lifecycle of a medicine

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
5.1	**Pharmacology, mechanism of action** • Non-clinical PK/PD and its impact on first in man studies • In vitro/in vivo correlations • Development. validation and use of methods • Proof of concept **Secondary pharmacology** • The relevance of pharmacology for toxicological development • The basis for selection of experimental animal models for safety studies.	1. Recognise, distinguish and propose the type of non-clinical development/study requirements according to the proposed use of the medicinal substance (both chemical and biological substances) 2. Recognise, distinguish and propose the type of non-clinical studies required at different stages of development 4. Evaluate and manage how the non-clinical issues are addressed in the regulatory submission dossiers
5.2	**The safety pharmacology and toxicity and their impact on use in humans** • Safety Pharmacology • Non-clinical ADME, toxicokinetics,/ metabolism • Toxicological qualification of impurities • General (single or repeated dose) toxicity testing and their impact on first in man studies and thereafter • Genotoxicity and its impact on clinical development • Carcinogenicity and impact on long-term clinical use • Toxicity to Reproduction and development and their impact on women and men in their reproductive age • Predictive biomarkers of human and animal toxicity	1. Recognise, distinguish and propose the type of non-clinical development / study requirements according to the proposed use of the medicinal substance (both chemical and biological substances) 2. Recognise, distinguish and propose the type of non-clinical studies required at different stages of development 4. Evaluate and manage how the non-clinical issues are addressed in the regulatory submission dossiers 5. Determine and manage how the non-clinical study findings are reflected in the product information and the Risk Management Plan 6. Predict, revise and evaluate the potential requirement for additional non-clinical studies during the lifecycle of a medicine
5.3	**Moving from non-clinical to clinical studies** • Specifics of preclinical studies in support of first in humans studies (determination of doses, etc) • Specifics of preclinical studies to support clinical trials in special patient populations (e.g. preclinical studies with juvenile animals) • Requirements for biopharmaceuticals as compared to small molecules	1. Recognise, distinguish and propose the type of non-clinical development / study requirements according to the proposed use of the medicinal substance (both chemical and biological substances) 2. Recognise, distinguish and propose the type of non-clinical studies required at different stages of development 4. Evaluate and manage how the non-clinical issues are addressed in the regulatory submission dossiers 5. Determine and manage how the non-clinical study findings are reflected in the product information and Risk Management Plan

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
		6. Predict, revise and evaluate the potential requirement for additional non-clinical studies during the lifecycle of a medicine

5.4	**Regulatory requirements for non-clinical data**
	• Principles of non-clinical development
	  ○ rationale for GLP
	  ○ procedures and relevant guidelines, ICH and ICH-guidelines
	  ○ 3Rs (Reduce, Refine, Replace)
	• Additional requirements for non-standard assays and species
	• CTD for Nonclinical studies
	  ○ Structure and peculiarities of the nonclinical Overall Summary, Tabulated Study Reports (within CTD Module 2)
	  ○ Structure of the Nonclinical Dossier (CTD Module 4)
		1. Recognise, distinguish and propose the type of non-clinical development / study requirements according to the proposed use of the medicinal substance (both chemical and biological substances)
		2. Recognise, distinguish and propose the type of non-clinical studies required at different stages of development
		3. Appreciate when an environmental risk assessment is required

5.5	**Other studies which need to be considered** • Environmental risk assessment • The development of Paediatric Medicines (Paediatric Investigation Plans) • Juvenile animal studies • Particular aspects of medicines for geriatric patients. • Local tolerance • Phototoxicity testing • Toxicological qualification of impurities • Safety assessment of new technologies (e.g. nanotechnology, gene therapy, transplantation products)	1. Recognise, distinguish and propose the type of non-clinical development / study requirements according to the proposed use of the medicinal substance (both chemical and biological substances) 2. Recognise, distinguish and propose the type of non-clinical studies required at different stages of development 4. Evaluate and manage how the non-clinical issues are addressed in the regulatory submission dossiers 5. Determine and manage how the non-clinical study findings are reflected in the product information and the Risk Management Plan 6. Predict, revise and evaluate the potential requirement for additional non-clinical studies during the lifecycle of a medicine
5.6	**Interpreting non-clinical data for clinical use** • Use of non-clinical data for designing clinical development programmes and post marketing studies • Impact on SmPC & PL • Impact on RMP and pharmacovigilance	4. Evaluate and manage how the non-clinical issues are addressed in the regulatory submission dossiers 5. Determine and manage how the non-clinical study findings are reflected in the product information and the Risk Management Plan 6. Predict, revise and evaluate the potential requirement for additional non-clinical studies during the lifecycle of a medicine

Module 6: Clinical Development

Module 6 Key messages

- Adequate clinical trial design and conduct are the basis for patient protection and data integrity in support of an MAA

LEARNING AIMS	
1.	Understand how clinical data are generated
2.	Understand how the GCP requirements help ensure the reliability and quality of the data integrity and patient safety
3.	Appreciate how clinical trial organization contributes to the efficiency of the clinical development programme
4.	Appreciate how exploratory studies differ from confirmatory studies and the different roles of these in supporting an MAA
5.	Appreciate how the results of clinical studies may impact on labeling claims
6.	Understand the regulatory requirements to ensure GCP and smooth conduct of a clinical trial

LEARNING OUTCOMES	
After successful completion of this module, the student should be able to:	
1.	Discuss why adequate and appropriate clinical trial design and conduct according to GxP are needed for patient protection, data integrity and regulatory acceptability
2.	Appraise, interpret and apply clinical trials legislation and related guidelines for effective implementation of a clinical trial programme
3.	Discuss the ethical, legal, scientific and practical aspects which need to be considered in undertaking clinical trials.
4.	Evaluate and manage how the clinical issues are addressed in the regulatory submission dossiers
5.	Describe and manage how the clinical study findings are translated into the product information
6.	Evaluate, predict and revise the potential requirements for additional clinical studies during clinical development

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
6.1	**Introduction to clinical trials and their design** • Clinical trial phases and types and "packages" • Non-interventional/observational studies • Quality of Life instruments • Epidemiological studies • Large simple clinical trials • Peculiarities of Medical Device trials • HTA assessments	1. Discuss why adequate and appropriate clinical trial design and conduct according to GxP are needed for patient protection, data integrity and regulatory acceptability 3. Discuss the ethical, legal, scientific and practical aspects which need to be considered in undertaking clinical trials. 6. Evaluate, predict and revise the potential requirements for additional clinical studies during clinical development
6.2	**Ethics in clinical research** • Ethical principles and dilemmas in clinical research • Declaration of Helsinki • Informed consent, incl. Informed Consent in vulnerable populations • Ethics committee systems • Confidentiality and data protection • Misconduct and fraud	1. Discuss why adequate and appropriate clinical trial design and conduct according to GxP are needed for patient protection, data integrity and regulatory acceptability 3. Discuss the ethical, legal, scientific and practical aspects which need to be considered in undertaking clinical trials.
6.3	**Good Clinical Practice (GCP)** • Guidelines (ICH-E6 and others) • Essential documents • Trial Master File (TMF) and archiving • Quality management in clinical trials – from QC to Quality Assurance / quality risk management and inspections (see also Module 10) • Application of Quality by Design principles to clinical trials	1. Discuss why adequate and appropriate clinical trial design and conduct according to GxP are needed for patient protection, data integrity and regulatory acceptability 2. Appraise, interpret and apply clinical trials legislation and related guidelines for effective implementation of a clinical trial programme 3. Discuss the ethical, legal, scientific and practical aspects which need to be considered in undertaking clinical trials.
6.4	**European Clinical Trial Legislation (EudraLex Vol. X)** • Clinical Trials Directive and related guidelines • GCP Directive • EudraCT database and registries • Clinical Trial Authorisation incl. IMPD • Ethical review process in the EU • Safety reporting and EudraVigilance database	1. Discuss why adequate and appropriate clinical trial design and conduct according to GxP are needed for patient protection, data integrity and regulatory acceptability 2. Appraise, interpret and apply clinical trials legislation and related guidelines for effective implementation of a clinical trial programme 3. Discuss the ethical, legal, scientific and practical aspects which need to be considered in undertaking clinical trials. 4. Evaluate and manage how the clinical issues are addressed in the regulatory submission dossiers 5. Describe and manage how the clinical study findings are translated into the product information

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
		6. Evaluate, predict and revise the potential requirements for additional clinical studies during clinical development
6.5	**Regulatory perspective on operational aspects of clinical trial design and conduct** • Feasibility of clinical research: regulatory requirements for clinical data From single studies to compilation of complete programmes • Investigator Brochure/IMPD • Protocol, CRF – reference to CT-design • Parties and responsibilities • Study management incl. human and financial resources • Site management incl. feasibility and recruitment • Contracts and insurance • Study medication preparation and handling / GMP (see also Module 4) • Safety assessment and documentation • Monitoring • Data evaluation and reporting • Statistical concepts and data review process • Acceptability of data for regulatory purposes • PIP • Clinical development guidelines • Outsourcing	1. Discuss why adequate and appropriate clinical trial design and conduct according to GxP are needed for patient protection, data integrity and regulatory acceptability 2. Appraise, interpret and apply clinical trials legislation and related guidelines for effective implementation of a clinical trial programme 3. Discuss the ethical, legal, scientific and practical aspects which need to be considered in undertaking clinical trials. 6. Evaluate, predict and revise the potential requirements for additional clinical studies during clinical development
6.6	**Translating clinical trial results into Product Information** • Structure and compilation of the clinical dossier • Selection and placement of data/assessment for inclusion into Product Information (Summary of Product Characteristics, Package Leaflet, labelling)	5. Describe and manage how the clinical study findings are translated into the product information

Module 7: Pharmacovigilance: from Classic Pharmacovigilance to Managing Benefit-Risk

Module 7 Key messages:

- Safety data generated by clinical development programmes is necessarily limited and experience in this setting does not provide comprehensive information on the safety of a new medicinal product in wider use
- Pharmacovigilance and control of medicines' use are required throughout the lifecycle of a product, before and after marketing authorisation
- The accruing safety data are to be interpreted in relationship to the benefits of the product as part of the continuous assessment of benefit and risk
- A safety risk management plan is required for marketing authorization. It is advisable to start this in the early stages of a product's life cycle as part of the long-term safety risk management strategy for a product. As a dynamic document, it requires regular updating, as a minimum, at the time of the DSUR and (post-authorization) the PSUR
- Close, procedural and timely interactions between Regulatory Affairs, Clinical and Pharmacovigilance/Drug Safety are necessary to ensure appropriate safety risk management of products

LEARNING AIMS	
1.	Appreciate the pharmacovigilance requirements to enable / facilitate regulatory compliance
2.	Appreciate the implications of pharmacovigilance information and its impact on product information and product usage (e.g. restrictions on use, suspension of product from market etc)
3.	Appreciate the need to review and revise risk management activities in the light of new information
4.	Appreciate when it is appropriate to communicate with Regulatory Agencies, Health Care Professionals, patients and other relevant stakeholders on new pharmacovigilance information

LEARNING OUTCOMES	
After successful completion of this module, the student should be able to:	
1.	Explain the EU regulatory requirements for pharmacovigilance to enable regulatory compliance in the interest of public health
2.	Discuss the roles of the various stakeholders in pharmacovigilance including the role of the EU-QPPV
3.	Distinguish the pharmacovigilance documentation (single case reports as well as aggregate reports such as DSUR and PSUR), tools and procedures pre- and post-approval
4.	Explain the role of the Risk Management Plan (RMP) including post-approval commitments, how to update it and evaluate its strategic implementation during the lifecycle of a medicinal product
5.	Explain the regulatory need for, and implications of, ongoing benefit-risk assessment of a medicinal product throughout its lifecycle, and describe the regulatory contribution to, and actions resulting from, such assessments
6.	Identify, devise and co-ordinate appropriate communications to relevant stakeholders on new pharmacovigilance information

7.	Compare and contrast the EU pharmacovigilance requirements with other ICH regions
8	Describe and manage how the non-clinical and clinical study safety findings are translated into the product information and communicated to the stakeholders

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	**LEARNING OUTCOME(S)**
7.1	**Introduction to pharmacovigilance:** • From preclinical safety to clinical safety • Benefit-risk evaluation in the clinical development and postmarketing phases • Pharmacovigilance Regulatory and Procedural Requirements	1. Explain the EU regulatory requirements for pharmacovigilance to enable regulatory compliance in the interest of public health
7.2	**European and national legal and administrative aspects and responsibilities** • Legal basis • Guidelines (EU legislation, Eudralex Volume 9A/Good Vigilance Practices) • Role of Pharmacovigilance Risk Assessment Committee (PRAC) • Information exchange within Europe • Information exchange beyond Europe • Inspections	1. Explain the EU regulatory requirements for pharmacovigilance to enable regulatory compliance in the interest of public health 7. Compare and contrast the EU pharmacovigilance requirements with other ICH regions
7.3	**Practical organisation and conduct of pharmacovigilance** • MAH's Pharmacovigilance System • Obligations of Marketing Authorisation Holders and Competent Authorities • Qualified Person for Pharmacovigilance (QPPV) • Quality system requirements	2. Discuss the roles of the various stakeholders in pharmacovigilance including the role of the EU-QPPV
7.4	**Reference safety information** • Investigator Brochure (IB) • Company Core Safety Information (CCSI) • Company Core Data Sheet (CCDS) • Relationship to SmPC • Legal implications	8. Describe and manage how the non-clinical and clinical study safety findings are translated into the product information and communicated to the stakeholders
7.5	• **Reporting obligations and definitions**Seriousness • (Un-)Expectedness • (Un-)Labelled • Spontaneous/(Un-)Solicited • Case origin (clinical trials/marketed product)s) • Causality assessment • Analysis of Similar Events (ASIME) • Periodic Safety Reports (PSUR/DSUR): structure, content, planning, follow-up • National, EU, ICH-regions,	1. Explain the EU regulatory requirements for pharmacovigilance to enable regulatory compliance in the interest of public health

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
7.6	**Pharmacovigilance toolkit** • Classic methods of signal detection • Registries, postmarketing trials, database studies, post-approval safety studies (PASS) • Epidemiological studies • Other data sources • New trends in pharmacovigilance	3. Distinguish the pharmacovigilance documentation (single case reports as well as aggregate reports such as DSUR and PSUR), tools and procedures pre- and post-approval
7.7	**Regulatory action and procedures** • Safety variations • Urgent Safety Restrictions • Referrals	5. Explain the regulatory need for, and implications of, ongoing benefit-risk assessment of a medicinal product throughout its lifecycle, and describe the regulatory contribution to, and actions resulting from such assessments 8. Describe and manage how the non-clinical and clinical study safety findings are translated into the product information and communicated to the stakeholders
7.8	**Risk and its management** • Safety risk management: identification, assessment, minimization, communication • Product specific Risk Management Plan (RMP): need, proposal, development, preparation, implementation, effectiveness, impact • The scope of the RMP – including follow-up of commitments. Relationship with Periodic Safety Reports (PSUR and DSUR) • Pre- and post-marketing research activities : Development RMP, Risk-Benefit Management Plan from Clinical Trials to Postmarketing	4. Explain the role of the Risk Management Plan (RMP) including post-approval commitments, how to update it and evaluate its strategic implementation during the lifecycle of a medicinal product 8. Describe and manage how the non-clinical and clinical study safety findings are translated into the product information and communicated to the stakeholders
7.9	**Risk communication (e.g. direct healthcare professionals communication, Urgent Safety Restriction)** • Benefit-risk communication to all stake-holders (why, what and when) • Building the concept of safe use of medicinal products • Benefit-risk by indication at the individual and population level • Pharmacovigilance crisis management	5. Explain the regulatory need for, and implications of, ongoing benefit-risk assessment of a medicinal product throughout its lifecycle, and describe the regulatory contribution to, and actions resulting from such assessments 6. Identify, devise and co-ordinate appropriate communications to relevant stakeholders on new pharmacovigilance information

Module 8: Regulatory Strategic Planning prior to Initial Marketing Authorisation

Module 8 Key messages:

- The Target Product Profile (TPP) is the basis for a clinical development programme. This is adapted during the development lifecycle as circumstances change and new data become available
- The TPP is shaped by multiple drivers, including proposed therapeutic use, regulatory, commercial and manufacturing considerations, as well as pricing and reimbursement.
- Clinical trial data from a clinical development programme help establish efficacy and safety and provide the basis for the assessment of benefit and risk in the studied indications
- The dossier compiled in support of a Marketing Authorization Application (MAA) should be designed to optimally support a benefit-risk assessment

LEARNING AIMS	
1.	Appreciate the risk/ benefit considerations for NCEs
2.	Appreciate the risk/ benefit considerations for specific product types and their impact on dossier requirements a. Paediatric medicines (e.g. formulation) b. Drug-Device combinations c. Vaccines (pandemic, preventative, therapeutic) d. Biologicals and biosimilars e. Advanced technology products
3.	Appreciate the need for and requirements of due diligence to assess new products and/or for licensing in products developed by third parties
4.	Understand how the clinical development programme relates to the Marketing Authorization Application (MAA)
5	Appreciate the need to address the clinical development programme as a whole, and its change over time, in the MAA dossier and to present this clearly to facilitate the regulatory assessment
6.	Provide the regulatory input to the clinical development programme design to ensure that regulatory requirements for the respective Target Product Profile (TPP) are met
7.	Appreciate when it is appropriate to seek Scientific Advice
8.	Understand the difference between promotion and scientific information and training

LEARNING OUTCOMES	
After successful completion of this module, the student should be able to:	
1.	Select and apply appropriate regulatory clinical development / study requirements according to the proposed use of the medicinal product
2.	Devise and assemble the elements and process of the clinical development plan

3.	Identify regulatory and business considerations which may drive the decision-making process during medicines development and assess their impact
4.	Evaluate opportunities for alternative approaches, compared with conventional approaches, to medicines development
5.	Manage strategic considerations for specific product types/ patient populations
6.	Categorize communication material and devise communication plans for different stakeholder groups

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	**LEARNING OUTCOME(S)**
8.1	**Defining the Target Product Profile (TPP)** • Proposed therapeutic use • Impact of marketing, commercial considerations and requirements • Manufacturing considerations • Pricing and reimbursement • Health Technology Assessments (HTAs) • Managing the TPP during the development lifecycle	1. Select and apply appropriate regulatory clinical development / study requirements according to the proposed use of the medicinal product 2. Devise and assemble the elements and process of the clinical development plan 3. Identify regulatory and business considerations which may drive the decision-making process during medicines development and assess their impact 4. Evaluate opportunities for alternative approaches, compared with conventional approaches, to medicines development 5. Manage strategic considerations for specific product types/ patient populations
8.2	**Regulatory considerations in constructing the Clinical Development Plan in alignment with the Target Product Profile (TPP)** • Exploratory development – Study objectives, endpoints and designs and statistical concepts in exploratory development – From pre-clinical proof of concept to First-in-Man to clinical Proof-of-Concept – Efficacy in exploratory development – Safety in exploratory development – Conventional vs. alternative strategies in development • The importance of dose-finding for efficacy and safety and impact on posology advice – Confirmatory clinical trials: – Objectives, endpoints, designs and statistical concepts – Target patient populations – Efficacy in confirmatory development	1. Select and apply appropriate regulatory clinical development / study requirements according to the proposed use of the medicinal product 2. Devise and assemble the elements and process of the clinical development plan 3. Identify regulatory and business considerations which may drive the decision-making process during medicines development and assess their impact 4. Evaluate opportunities for alternative approaches, compared with conventional approaches, to medicines development 5. Manage strategic considerations for specific product types/ patient

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
	– Safety in confirmatory development • Drug-drug interactions - how they occur and when they are important • Relevant guidelines • Scientific Advice (see also Module 3) • Impact of the Paediatric Investigation Plan (PIP) • Impact on compassionate use programs (NB: off-label use is implicitly addressed in this context)	populations
8.3	**Regulatory submission strategy** • Advantages and disadvantages of different submission routes • Presentation of "pipeline" to authorities • Special consideration for Small and Medium sized Enterprises (SMEs) • Contingency planning, including impact of follow up measures • Pre-submission Communication with Competent Authorities • Development of key indications	3. Identify regulatory and business considerations which may drive the decision-making process during medicines development and assess their impact 4. Evaluate opportunities for alternative approaches, compared with conventional approaches, to medicines development 5. Manage strategic considerations for specific product types/ patient populations 6. Categorize communication material and devise communication plans for different stakeholder groups
8.5	**Communication: planning and implementation** • Publication strategy • Promotional material and advertisement claims • Communication with patient and other stakeholder groups	6. Categorize communication material and devise communication plans for different stakeholder groups
8.6	**Strategic considerations for specific product types and populations** • Combination medicinal products (drug-drug, drug-device, etc) • Paediatric medicines, geriatrics, women of child-bearing potential • Orphan drugs • Generics	3. Identify regulatory and business considerations which may drive the decision-making process during medicines development and assess their impact 4. Evaluate opportunities for alternative approaches, compared with conventional approaches, to medicines development 5 Manage strategic considerations for specific product types/ patient populations

Module 9: Regulatory Strategic Planning and Life Cycle Management after Initial Marketing Authorization

***Module 9 Key messages**:*

- To appreciate the need for a continuous product development lifecycle, taking into account commercial aspects, expansion of the patient population eligible for treatment, new indications, new formulations, new methods of manufacture, patent protection and legal status
- To appreciate the need for MA maintenance to accommodate scientific advances and ongoing/changing regulatory requirements, as well as safety / pharmacovigilance and risk minimization requirements

LEARNING AIMS	
1.	Understand which rules must be followed absolutely and where there is room for manoeuvre to ensure regulatory compliance
2.	Appreciate the need to evaluate and use new information in the context of a product's use, whilst maintaining regulatory compliance
3.	Understand how promotional activity is limited by the underlying SmPC
4.	Understand regulatory opportunities to expand the market (pediatric use, new indications, legal status changes, new formulations, use of new technologies)
5.	Understand the need for and approaches to manage loss of exclusivity
6.	Appreciate the need to solve problems and understand the mechanisms available to do this (HCP letters, product batch recall etc)
7	Understand the impact of regulatory action in maintaining market supply (e.g. turn- around times on changes to production, and product information to implement changes)
8.	Understand the importance of maintaining appropriate and clear Patient Information

LEARNING OUTCOMES	
After successful completion of this module, the student should be able to:	
1.	Appraise and assemble key elements of the lifecycle management plan
2.	Identify regulatory and business considerations which may affect the lifecycle management
3.	Plan for, prepare and implement the necessary regulatory procedures for the continuous product development during the lifecycle of a medicine
4.	Select and apply appropriate regulatory data requirements according to the proposed change to the medicinal product
5.	Construct a plan for management of complaints, recalls, safety issues during the lifecycle of a medicine
6	Differentiate between promotional and educational activities and ensure consistency of both with the product information
7.	Identify, devise and manage appropriate communications to relevant stakeholders according to the intended population, disease type, clinical usage, etc.

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	LEARNING OUTCOME(S)
9.1	**Drivers for life cycle management** • Optimizing efficacy and patient protection • Expanding the patient population eligible for treatment (e.g. pediatric patients) • Regulatory requirements • Forecasting product revenues • Expanding/protecting market share and addressing local commercial considerations • Managing the SmPC • Manufacturing considerations • Pricing and reimbursement • Health Technology Assessments (HTAs) • Managing patent protection/exclusivity	1. Appraise and assemble key elements of the lifecycle management plan 2 Identify regulatory and business considerations which may affect the lifecycle management 3. Plan for, prepare and implement the necessary regulatory procedures for the continuous product development during the lifecycle of a medicine 4. Select and apply appropriate regulatory data requirements according to the proposed change to the medicinal product
9.2	**Maintenance and lifecycle: dossiers and procedures** • Line extensions • Variations • Risk minimisation procedures and follow up measures (post-approval commitments) • Abridged applications • Generic products • Sunset clause/renewal • Changes to legal status	1. Appraise and assemble key elements of the lifecycle management plan 2. Identify regulatory and business considerations which may affect the lifecycle management 3. Plan for, prepare and implement the necessary regulatory procedures for the continuous product development during the lifecycle of a medicine 4. Select and apply appropriate regulatory data requirements according to the proposed change to the medicinal product
9.3	**Actions driven by Regulatory Authorities** • Reports and product complaints • Community procedures (risk, harmonization of indications, differing national decisions) • Harmonization procedures (including core Summary of Product Characteristics, core package leaflets) • Quality defects and risk management	4. Select and apply appropriate regulatory data requirements according to the proposed change to the medicinal product 5. Construct a plan for management of complaints, recalls, safety issues during the lifecycle of a medicine 7. Identify, devise and manage appropriate communications to relevant stakeholders according to the intended population, disease type, clinical usage, etc

9.4	**Portfolio planning and management** • Paediatric development • New galenic formulations • Combination products • New indications	1. Appraise and assemble key elements of the lifecycle management plan 2. Identify regulatory and business considerations which may affect the lifecycle management 3. Plan for, prepare and implement the necessary regulatory procedures for the continuous product development during the lifecycle of a medicine 4. Select and apply appropriate regulatory data requirements according to the proposed change to the medicinal product
9.5	**Communication with stakeholders** • Interaction between manufacturers and health care providers (e.g. information, training, “Dear Doctor” letters) • Format and presentation of information communication, depending on the product, type of therapy, treatment indication and business • Promotional vs. educational communications • Voluntary Codes of Practice vs. compulsory Rules	5. Construct a plan for management of complaints, recalls, safety issues during the lifecycle of a medicine 6. Differentiate between promotional and educational activities and ensure consistency of both with the product information 7. Identify, devise and manage appropriate communications to relevant stakeholders according to the intended population, disease type, clinical usage, etc

Module 10: Quality Management and Inspections

Module 10 Key messages:
To understand how to

- Apply the principles of Quality Management, Risk Management and Quality by Design (QbD)
- Provide evidence of compliance with Good Practice Standards
- Support inspection readiness and, as appropriate, the organization of inspections and escorting inspectors
- React in case of detection of serious deviations or non-compliance by establishing an action plan (GLP) or performing a root-cause analysis and implementing corrective and preventive actions and communicate adequately in these situations with regulatory authorities

LEARNING AIMS	
1.	Understand the public health implications of failure of good practice / quality management in Pharmaceutical Industry and Regulatory Agencies
2.	Understand the regulatory requirements to ensure compliance with GxP
3.	Understand the role of training and development to ensure compliance with regulatory requirements
4	Understand the role of Quality Risk Management and Quality by Design

LEARNING OUTCOMES	
At the end of this module, the student should be able to:	
1.	Discuss, interpret and apply the principles and key elements of a quality management system and understand its role in ensuring compliance with GxP
2.	Assess and discuss how a quality management system contributes to good regulatory practices in industry and Competent Authorities
3.	Understand and apply Quality Risk Management / Quality by Design and its impact on regulatory (in-house and regulatory authorities) decision making
4.	Describe the purpose and scope of inspections by Competent Authorities, and the prerequisites for inspection readiness
5.	Understand how inspections contribute to make key elements of a quality management system robust, ensure compliance with GxP, ensure protection of patients' safety, rights and integrity, as well as data integrity, environmental protection and animal welfare as laid down in GxP regulations
6.	Discuss and develop a strategy for the involvement of Regulatory Affairs in audit and inspection follow-up and how to prepare and implement a corrective and preventive action plan
7.	Discuss and describe the similarities and differences of GCP, GLP, GMP and QA/QC standards and processes in pharmacovigilance
8.	Understand and develop a risk / issue management and business continuity plans for a given area, address cross-functional challenges and develop a holistic communication strategy

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	**LEARNING OUTCOME(S)**
10.1	**Quality management (QM) principles** • Evolution and scope • Models and standards • Design and implementation of a QM system (QMS) • Change management strategies when a QMS is introduced / updated • Development of SOPs • Training of/with SOPs • Knowledge management and its documentation • Quality Risk Management/Quality by Design • Delegation of tasks vs delegation of responsibility	1. Discuss, interpret and apply the principles and key elements of a quality management system and understand its role in ensuring compliance with GxP 2. Assess and discuss how a quality management system contributes to good regulatory practices in industry and Competent Authorities 3. Understand and apply Quality Risk Management / Quality by Design and its impact on regulatory (in-house and regulatory authorities) decision making 4. Describe the purpose and scope of inspections by Competent Authorities, and the prerequisites for inspection readiness 6. Discuss and develop a strategy for the involvement of Regulatory Affairs in audit and inspection follow-up and how to prepare and implement a corrective and preventive action plan
10.2	**Quality assurance (QA) and quality control (QC) in the pharmaceutical industry** • Pharmaceutical development and manufacturing • Preclinical development • Clinical development • (Bio) Laboratories • Pharmacovigilance • Data Management • Audits and CAPAs • Electronic systems, including Computerized Systems Validation (CSV)	1. Discuss, interpret and apply the principles and key elements of a quality management system and understand its role in ensuring compliance with GxP 2. Assess and discuss how a quality management system contributes to good regulatory practices in industry and Competent Authorities 6. Discuss and develop a strategy for the involvement of Regulatory Affairs in audit and inspection follow-up and how to prepare and implement a corrective and preventive action plan 7. Discuss and describe the similarities and differences of GCP, GLP, GMP and QA/QC standards and processes in pharmacovigilance

	THIS MODULE WILL ADDRESS THE FOLLOWING TOPICS	**LEARNING OUTCOME(S)**
10.3	**Inspections** • QM/QA (Inspectorates – Sponsor) • PIC/S (Pharmaceutical Inspection Convention and Co-operation Scheme) • Quality Manuals • European GMP inspections • European GCP inspections • European pharmacovigilance inspections • European GLP inspections and joint OECD inspections • Roles of the EMA and the national competent authorities • EU formats for Inspection Reports • FDA inspections and joint FDA/ EMA/ EU-MS inspections	4. Describe the purpose and scope of inspections by Competent Authorities, and the prerequisites for inspection readiness 5. Understand how inspections contribute to make key elements of a quality management system robust, ensure compliance with GxP, ensure protection of patients' safety, rights and integrity, as well as data integrity, environmental protection and animal welfare as laid down in GLP regulations
10.4	**Risk and crisis management** • Quality risk management according to ICH Q9 and in clinical research • Incident management and contingency planning • Business continuity plans • Managing the GxP and Pharmacovigilance interface in a recall situation • Issue management and communication with regulatory bodies and other stakeholders • Managing communication with the public at large	8. Understand and develop a risk / issue management and business continuity plans for a given area, address cross-functional challenges and develop a holistic communication strategy