UNIVERSITY of NICOSIA

Course Syllabus

Course Code	Course Title	ECTS Credits
PHAR-619	Clinical Trials, Preclinical and Clinical Development and Documentation	10
Prerequisites	**Department**	**Semester**
None	Health Sciences	Spring
Type of Course	**Field**	**Language of Instruction**
Compulsory	Pharmacy	English
Level of Course	**Lecturer(s)**	**Year of Study**
2nd Cycle	Drs Zampatis, Kitromilidou, Prapopoulou, Aislaitner, Zacharia, Calabrese	1st
Mode of Delivery	**Work Placement**	**Corequisites**
e-learning	--	none

Course Objectives:

Navigating the drug development process from early discovery to Phase I clinical trials can be complex and costly. While preclinical research answers basic questions about a drug's safety, it is not a substitute for studies of ways the drug will interact with the human body. "Clinical research" refers to studies, or trials, that are done in humans. As the developers design the clinical study, they will consider what they want to accomplish for each of the different Clinical Research Phases and begin the Investigational New Drug Process (IND), a process they must go through before clinical research begins. Clinical trials constitute a critical step in the development process that ensures marketing authorization.

The aim of the course is to cover clinical trials, the application of clinical and preclinical research principles. Moreover, the course will provide a thorough review of the requirements and critical elements related to the preclinical and clinical examinations, including the design of a technical document ("common technical document") for the preclinical part of the registration file and the necessary clinical documentation in the process of drug registration. Furthermore, the course will provide an understanding of the practical regulatory aspects of global clinical research, in order to offer effective advice on the regulatory issues likely to arise during clinical programs.

By the end of this course, students will be able to make plans and take decisions for preclinical and clinical development and documentation.

Learning Outcomes:

After completion of the course students are expected to be able to:

- Illustrate knowledge of the required clinical documentation for a Marketing Authorization
- Appraise, interpret and apply clinical trials legislation and related guidelines (EU Clinical Trial directive) for effective implementation of a clinical trial programme (application) and associated documentation
- Apraise the strategic role of clinical study reports and summaries in obtaining an optimal product label and product information
- Discuss the ethical, legal, scientific and practical aspects which need to be considered in undertaking clinical trials including potential requirements for additional clinical studies.
- Create, analyse and evaluate a regulatory strategy plan for the clinical development of a new drug
- Prepare and evaluate the documentation needed to fulfil the non-clinical part of a registration dossierDesign preclinical dossier examinations in accordance with the regulatory requirements including good laboratory practices (GLP

Course Content:

- Medicinal product regulations in the 21st century and Global regulatory requirements

o history and background to regulations of medicine, the legal basis of control by regulatory authorities, regulatory aspects of the clinical development programme, marketing applications, the future system of medicinal programme regulation, the regulatory environment in the USA)

- Clinical Trial protocol and clinical trial design

o the phases of a clinical development programme, trial design, the elements of trial design, designing a multicentre trial, definition and purpose of the protocol, writing a protocol, the main decisions to be made, administrative sections, protocol amendments

- Early phase studies, pharmacokinetics and adverse drug reaction

o Selection of volunteers, design of study, adverse effects, compartmental concept, administration, population pharmacokinetics, early phase drug interactions)

- Phase IV studies

o constraints, scientific method, regulatory basis of phase IV studies, comparative studies, new indication-dosage-formulation, secondary prevention studies, randomized studies evaluating safety

- Monitoring

o Study preparation, study initiation, study conduct and monitoring, study termination

- Drug safety in clinical studies and pharmacovigilance

o clinical studies, adverse effects, laboratory safety data, presentation of safety data, pharmacovigilance, case control studies, cohort studies, prescription event monitoring

- Trial master file

o responsibility for and management of the trial master file, the appearance of the trial master file, essential documents in the trial master file

- Overview of pharmacology, pharmacokinetic and toxicology
- Good Laboratory Practice and Quality on preclinical studies
- "First in Man: Pharmacology & Kinetics, dosage and Regimen, genotoxicity, toleranace and other studies"
- Ethical issues in clinical research, Fraud and misconduct.

o declaration of Helsinki, good clinical practice, ethical issues in clinical trial design, European Community good clinical practice guidelines

- Clinical study site management, audit and inspection

Learning Activities and Teaching Methods:

Teaching material including PowerPoint presentations with extended descriptions and explanations, asynchronous video presentations, additional readings (journal articles and ebooks), access to additional videos related to the course, synchronous meetings (WebEx), forums, chats, quizzes, case studies, wikis, and major assignments.

Assessment Methods:

Continuous Assessment (major assignments and weekly activities), Final Exam

Required Textbooks / Readings:

Title	Author(s)	Publisher	Year	ISBN
Principles and practice of clinical research.	Gallin, J. and Ognibene, F	Elsevier/AP.	2017	9780128499054 eBook ISBN: 9780128499047

Guideline for good clinical practice E6(R2).1 December 2016 EMA/CHMP/ICH/135/1995		Committee for Human Medicinal Products	2016	
Fundamentals of clinical trial design,	Scott R. Evans		2010	J Exp Stroke Transl Med. 2010 January 1; 3(1): 19–27
ICH HARMONISED GUIDELINE INTEGRATED ADDENDUM TO ICH E6(R1): GUIDELINE FOR GOOD CLINICAL PRACTICE		ICH	2015	
Guideline on the content, management and archiving of the clinical trial master file (paper and/or electronic) EMA/INS/GCP/856758/2018		Good Clinical Practice Inspectors Working Group (GCP IWG)	2018	
Preclinical Development Handbook. ADME and Biopharmaceutical properties. (2008)	Gad, S	John Wiley & Sons	2008	9780470249031
Designing Clinical Research FOURTH EDITION	Stephen B. Hulley,	LIPPINCOTT WILLIAMS & WILKINS, a WOLTERS KLUWER	2013	9781469840543
A comprehensive guide to toxicology in preclinical drug development.	Faqi, A	Elservier	2013	ISBN: 9780123878151 eBook ISBN: 9780123878168
Global approach in safety testing. New York.	Van Der Laan, J. & De George, J	Springer	2012	9781461459491
ICH Topic E 9 Statistical Principles for Clinical Trials. NOTE FOR GUIDANCE ON STATISTICAL PRINCIPLES	ICH	ICH	1998	

FOR CLINICAL TRIALS (CPMP/ICH/363/96				
COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS (CPMP) POINTS TO CONSIDER ON APPLICATION WITH 1. META-ANALYSES; 2. ONE PIVOTAL STUDY	CPMP	EMA	2001	
ADDENDUM ON ESTIMANDS AND SENSITIVITY ANALYSIS IN CLINICAL TRIALS TO THE GUIDELINE ON STATISTICAL PRINCIPLES FOR CLINICAL TRIALS E9(R1)		ICH	2019	
ICH Topic M 4 Q Common Technical Document for the Registration of Pharmaceuticals for Human Use - Quality Step 5	CMPM	EMA	2003	
PROCEDURE FOR CONDUCTING GCP INSPECTIONS REQUESTED BY THE EMEA GCP Inspectors Working Group. EMEA/INS/GCP/197223/2005		EMA	2005	