INTRODUCTION AND LEARNING OUTCOMES

The training course is intended for physicians, biopharmaceutical scientists and healthcare professionals working in exploratory medicines development research as well as investigators and research staff performing early phase clinical trials.

Learning Outcomes

At the end of this course participants will be able to address and apply the ethical, regulatory and quality requirements of early phase clinical trials in their daily work. They will be familiar with the required measures for risk identification, assessment, mitigation and management in the early phase clinical trial activities presented in this course. Participants will know how to prepare the single dossier documentation and how to interact with the Clinical Trial Information System (CTIS) within the new Clinical Trial Regulation framework. They will understand the organizational and quality requirements when preparing a Phase I unit for inspection readiness. Case studies and a home work will provide the opportunity to discuss and apply the theoretical background provided in the lectures.

Case studies

- Review of the Informed Consent Form - **blinded** Tegenero case *(homework and virtual Day 1)*
- Prepare a mock submission dossier according to EU CTR *(on-site on Day 3 at f2f meeting)*
- Homework: Review an 'old' protocol according to the new EU-CTR *(between Day 4 and 5)*
- Homework: Pre-reading and reading in-between course days; preparation of test

Pre-reading

- Declaration of Helsinki
https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

- ICH-Guidelines: refresh your mind on E6 R2 (GCP) and E8
https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice-scientific-guideline
https://www.ema.europa.eu/en/ich-e8-general-considerations-clinical-studies-scientific-guideline

- Familiarize yourself with the specific topics covered in the EU-CTR
https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-regulation

- GDPR (European General Data Protection Regulation), sections concerning clin. examinations)

- Familiarize yourself with the topics covered in EMA 'Guideline on computerised systems and electronic data in clinical trials' (EMA/INS/GCP/112288/2023);
https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-computerised-systems-electronic-data-clinical-trials_en.pdf

- Glossary on terms and definitions (EMA)

- FIH Guideline / FDA guidance documents for first-in-human dose

- Pre-course reading on marketing authorisation:
  - How are medicines evaluated at the EMA? booklet available from EMA
  - Clinical Trial Route Map – NIHR
http://www.ct-toolkit.ac.uk/routemap

- All documents for the mock submission dossier

- Blinded Tegenero informed consent form

programme modifications reserved - status 08/2024

FACULTY MEMBERS

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INFORMATION

Venue	Virtual via Microsoft Teams. *Guests receive personal login data.*	
Requirement	A Download of the MS Teams Desktop-App is highly recommended.	
and	**elaya hotel frankfurt oberursel** Zimmersmühlenweg 35 61440 Oberursel (Germany) (A room block is reserved - please feel free to book during your registration	
Dates	Day 1	29 November 2024 -Online-
	Day 2-4	2-4 December 2024 Oberursel (Germany)
	Day 5	9 December 2024 -Online-
Fees	1.900 EUR 1.500 EUR	Guest Member*

*of ACRON, AGAH, AHPPI, AFPT-CPI HEALIXIA, POLFEMED

CONTACT AND FURTHER INFORMATION

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Association for Applied Human Pharmacology

EUFEMED

Certificate/Diploma Course

in Human Pharmacology Module 3

Regulatory, operations, ethical and quality requirements in today's early phase clinical trials

29 November 2024, online

2- 4 December 2024, on-site (face-to-face)

9 December 2024, online

Day 1 · FRIDAY, 29 November 2024 (online)

09:00 - 09:15 **Introduction of faculty and participants**
Sybille Baumann, Kerstin Breithaupt-Grögler, Ingrid Klingmann

09:15 - 10:00 **Historical development of ethical standards:** Nuremberg Code, DoH, ICH-GCP, CIOMS
Nadja Faisst

10:00 - 11:15 **What needs to be regulated in a clinical trial?** Clinical trial approval application dossier with protocol, IB, IMPD, etc., approval by CA and EC, substantial modifications, IMP, Safety info, annual updates, results publication, QA, etc.
Ingrid Klingmann

11:15 - 11:30 Break

11:30 - 12:45 **The structure of clinical trial legislation in the** EU, UK, CH, and USA CTD, CTR, MHRA, Swissmedic, FDA; legal texts and guidelines
Birka Lehmann

12:45 - 13:00 **EudraLex Vol. 1,2,3,4,9,10**
Nadja Faisst

13:30 - 13:45 Break

13:45 - 15:00 **What is GxP?** Overview of key elements of GCP (Good Clinical Practice) and GMP (Good Manufacturing Practice), GLP (Good Laboratory Practice), GcLP (Good clinical Laboratory Practice) including sample management
Kerstin Breithaupt-Grögler
Karl Kleine

15:00 - 15:15 Break

15:15 - 16:45 **What is a quality management system in early phase clinical trials?** How to prepare the regulatory infrastructure for an early phase trial including risk assessment and management?
Thomas Schillinger

16:45 - 17:15 **Case discussion:** Informed consent process in Phase I - Tegenero ICF will be discussed
(Pre-reading of Tegenero case is mandatory!)
Kerstin Breithaupt-Grögler, Ingrid Klingmann

16:45 - 17:15 **Principles of EU-Clinical Trials Regulation**
Ingrid Klingmann

Day 2 · MONDAY, 2 December 2024 (face-to-face)

09:00 - 10:00 **Regulatory development strategy options** incl. central approval or country-specific approval, pre-approval scientific advice with EMA and/or FDA, abbreviated marketing authorisation (conditional approval, rolling review), interaction with CA and ECs, paediatric development obligations in EU and USA (PIP)
Birka Lehmann

10:00 - 11:00 **Principles of clinical trial authorization** according to the EU-CTR, German Research facilitation Act ('Medizinforschungsgesetz')
Ingrid Klingmann

11:00 - 11:15 Break

11:15 - 12:15 **An introduction to the CTR-related pharmaceutical regulatory framework for investigational medicinal products** (IMPs, small molecules) in early phase clinical trials
Susanne Trumm

12:15 - 13:00 **Translational considerations of non-clinical experience to human studies** incl. M3, safety, bioavailability, pharmacokinetics, and metabolism
Diana Sims-Silbermann

13:00 - 14:00 Break

14:00 - 15:00 **First-in-human guideline** with focus on determination of first dose, process for dose escalation decisions, stopping rules, clinical safety (AE/SAEs), ‚trend assessment processes' regarding safety, PK and PD, independent data monitoring committee; FDA guidance documents for first-in-human dose
Kerstin Breithaupt-Grögler

15:00 - 15:45 **Sponsor procedures** concerning risk identification, risk mitigation, risk management, risk-based monitoring.
Karin Köhler-Hansner

15:45 - 16:00 Break

16:00 - 17:30 **Trial preparation in Phase 1:** the CTA application dossier (protocol, IB, IMPD), site selection, contracting and management of suppliers, investigator agreement, insurances
Diana Sims-Silbermann

17:30 - 18:00 **Q&A on today's topics**

Day 3 · TUESDAY, 3 December 2024 (face-to-face)

09:00 - 09:30 **How does a Sponsor** prepare the regulatory infrastructure for an early phase clinical trial? Which relevant documents are set up by the Sponsor?
Karin Köhler-Hansner

09:30 - 11:15 **Which documents are required for clinical trial authorisation application?** Cover letter, trial protocol, informed consent, IB, IMPD, manufacturing authorization, site suitability template, recruitment arrangements, proof of insurance, financial arrangements, proof of payment, compliance statement GDPR
Maria Anschütz, Kerstin Breithaupt, Nadja Faisst, Sylvia Grebe, Burkhard Kerlin

11:15 - 11:30 Break

11:30 - 12:15 **Clinical trial authorisation application: redaction and deferrals**
Burkhard Kerlin

12:15 - 13:15 Break

13:15 - 15:00 **Which information needs to be redacted? Break-out groups:** redaction of trial protocol, informed consent, IB/IMPD, site suitability document, taking into account the respective chapters of EU-CTR

15:00 - 15:15 Break

15:15 - 18:30 **CTIS Training module:**
- Explanation of CTIS structure, available trainings, timelines, organisational aspects between regulatory and operations departments
- Upload of a mock CTA submission dossier according to the EU CTR
- Documents to be uploaded following the end of trial (e.g., upload of scientific results summary, lay summary of results)
Maria Anschütz, (Sybille Baumann), Kerstin Breithaupt-Grögler, (Nadja Faisst), Sylvia Grebe, Burkhard Kerlin, Ingrid Klingmann, Diana Sims-Silbermann

19:00 **Joint Dinner with participants and faculty**

Day 4 · WEDNESDAY, 4 December 2024 (face-to-face)

09:00 - 10:15 **Organisation and responsibilities of an early phase trial unit:** Set-up of Phase I unit, infrastructure, how to be ready for a pre-qualification visit, subject recruitment, data protection, informed consent, housing conditions, ethical and technical aspects of assessments, data management, remuneration, follow-up (FiH guideline in practical application, Eudralex guidance for inspections)
Sybille Baumann

10:15 - 11:00 **Discussion / Short case study**
Sybille Baummann

11:00 - 11:15 Break

11:15 - 12:45 **Standard operating procedures in an early phase trial unit** SOP system from recruitment to sample management, 'Mind Map'
Thomas Schillinger

12:45 - 13:45 Break

13:45 - 15:00 **Evaluation and reporting of a Phase 1 trial in the EU (**Statistical analysis plan, clinical study report, start-end, summary of clinical trials, Lay summary)
Kerstin Breithaupt-Grögler

15:00 - 15:15 Break

15:15 - 15:45 **Clinical trial transparency:** Registration of clinical trials in EU and globally, reporting of results in data bases
Nadja Faisst

15:45 - 16:15 **Joint discussion**
Challenges of transparency in Phase 1 trials

Home work Individually or as group work with up to 4 participants: Check the trial protocol that was developed under the EU Directive versus the requirements of the EU clinical trials regulation and identify the required changes.

Day 5 · MONDAY, 9 December 2024 (online)

09:00 - 09:30 **Feedback from home work on trial protocol adaptation**

09:30 - 11:00 **Pharmacovigilance in clinical trials** (Safety reporting, Serious breaches, MedDRA coding, SUSAR reporting in EudraVigilance, IND safety reporting, DSUR, periodic safety reports)
Maria Weber

11:00 - 11:15 Break

11:15 - 12:15 **Validation** - PK and PD assessments, bioanalytical methods, computerised systems and data capture
Karl Kleine

12:15 - 13:00 Break

13:00 - 14:00 **Document management**
TMF, ISF, archiving conditions
Diana Sims-Silbermann

14:00 - 14:45 **Sponsor's study oversight** including cross-discipline due diligence and monitoring for all protocol-contracted out services, outsorcing of sponsor obligations, 'vendor assessment'
Karin Köhler-Hansner

14:45 - 15:00 Break

15:00 - 16:00 **How to prepare audit and inspection readiness at the trial site?** Examples regarding Inspection Findings
Thomas Schillinger

16:00 - 17:00 **Audit, audit response (CAPA), inspection**
Karl Kleine

17:00 - 17:15 Feedback

17:15 - 18:15 Final Test (mandatory)