

5th – 9th December 2011 & 12 th – 13 th December 2011

Base Module 4: Clinical Trials

Room: 105 Laennec - Mon. Dec 5

**9 a.m. – 12.30 p.m. - Catherine Cornu, Rabia Berthier-Marsou
& 2 p.m. - 5 p.m.**

QUALITY MANAGEMENT SYSTEM

5p.m. – 6.30 p.m. – Maan Zrein

ORPHAN DRUGS, PAEDIATRICS, ADVANCED THERAPIES, GENERICS & BIOSIMILARS (PART1)

Rockefeller - Tues. Dec 6

JOURNEE IPIL CF PROG

Room: 104 Laennec -Wed. Dec 7

9 a.m. – 12.00 p.m. – Yannick Pletan

CHOICE OF TRIAL DESIGN

NEW TRIAL DESIGNS

NON-INTERVENTIONAL / OBSERVATIONAL STUDY DESIGN

INVESTIGATOR BROCHURE

PROTOCOL PREPARATION & REVIEW

TRIAL MASTER FILE (TMF)

CLINICAL TRIAL REPORT

2p.m. – 5 p.m. – Delphine Bertram

ADVERSE EVENT ASSESSMENT & REPORTING

STUDY MEDICATION HANDLING & DRUG ACCOUNTABILITY

5P.M. – 6.30 P.M. – MAAN ZREIN

**ORPHAN DRUGS, PAEDIATRICS, ADVANCED THERAPIES,
GENERICS & BIOSIMILARS (PART2)**

Room: 100 a.m. / Room: of thesis p.m.-Thurs. Dec 8

9 a.m. – 12.00 p.m. & 1 p.m. - 4 p.m. - Ton Cleophas

**DATA MANAGEMENT & STATISTICS
OPTIONS FOR DATA COLLECTION
CASE REPORT FORM (CRF)
DATABASES, SOFTWARE VALIDATION, & ARCHIVING
FROM SOURCE DOCUMENT TO CRF COMPLETION
STATISTICS
STATISTICIAN
STATISTICAL ANALYSIS PLAN
TRIAL DESIGN
HYPOTHESIS TESTING
SAMPLE SIZE CALCULATION
MINIMISING BIAS
TYPES OF DATA & STANDARDISATION OF MEASUREMENT
PATIENT-REPORTED OUTCOMES**

**4 p.m. - 5 p.m. - Patrick Chevarier
DATABASES, SOFTWARE VALIDATION, & ARCHIVING**

Room: 100 Laennec-Fri. Dec 9

9 a.m. – 12.00 p.m. & 1 p.m. - 4 p.m.- Aeilko Zwinderman

**STATISTICAL ANALYSIS OF EFFICACY END-POINTS & SAFETY
INTERIM ANALYSIS
PAIRED AND NON-PAIRED TESTS, PARAMETRIC AND NON-PARAMETRIC TESTS
RATING AND VISUAL ANALOGUE SCALES, PATIENT DIARIES, & LABORATORY
VALUES
HANDLING OF MISSING DATA
SENSITIVITY & SPECIFICITY OF TESTS
TRUE & APPARENT INCIDENCE & PREVALENCE
INTERPRETATION OF ANALYSES; ASSESSMENT OF VIOLATIONS, WITHDRAWALS
ERRORS, BIAS
STATISTICAL REPORT WRITING
CLINICAL INTERPRETATION OF TRIAL RESULTS
DEALING WITH CONFOUNDING FACTORS & BIAS
CRITICAL REVIEW OF PUBLICATIONS**

**4 p.m. - 5 p.m. – Catherine Cornu
CLINICAL TRIAL REGISTRIES**

Development and Evaluation of Medicinal Products, Master Degree

Room: 106 - Mon. Dec 12

9 a.m. – 12.00 p.m. & 1 p.m. - 5 p.m. - Mickael Bone & Pierre Mallia

ETHICS AND LEGAL ISSUES

ETHICAL ISSUES IN BIOMEDICAL RESEARCH & PHARMACEUTICAL MEDICINE

ETHICS

PROTECTION OF RESEARCH SUBJECTS

ETHICAL ASPECTS IN RESEARCH QUESTIONS & STUDY DESIGNS

CONFLICT OF INTEREST & EQUIPOISE

ETHICAL ASPECTS OF SUBJECT CONTACT & RECRUITMENT

ETHICAL ISSUES OF REIMBURSEMENT, COMPENSATION, & INDUCEMENT

RISKS, BENEFITS, & BURDEN OF STUDY PARTICIPATION

INFORMED CONSENT PROCESS

Room: Amphi A2 -Tues. Dec 13

9 a.m. – 12.00 p.m. & 1 p.m. - 5 p.m. - Mickael Bone & Pierre Mallia

PRIVACY, CONFIDENTIALITY, & DATA PROTECTION

INDEMNITY & INSURANCE FOR PARTICIPANTS, INVESTIGATORS, INSTITUTIONS

ETHICAL ASPECTS OF STUDY FOLLOW-ON

ETHICAL ASPECTS OF TAKING TRIAL SAMPLES FOR GENOMIC & RELATED ANALYSES

ETHICAL ASPECTS OF CLINICAL TRIALS IN VULNERABLE POPULATIONS

ETHICAL ASPECTS OF ADVANCED THERAPY MEDICINAL PRODUCTS

ETHICAL ASPECTS OF CLINICAL TRIALS IN DEVELOPING COUNTRIES

FRAUD & MISCONDUCT

Room: -Wed. Dec 14

9 a.m. – 12.00 p.m. – Nicolas Leroy

FEASIBILITY & INVESTIGATOR RECRUITMENT

PRE-STUDY VISITS & INVESTIGATOR MEETINGS; INVESTIGATOR TRAINING

CONTRACTUAL ARRANGEMENTS WITH INVESTIGATORS

1p.m. – 5 p.m. – Tiphanie Ginhoux

WITHIN-TRIAL DECISIONS

MONITORING & SOURCE DOCUMENT VERIFICATION

GOOD CLINICAL PRACTICE (GCP)

OPTIONS FOR DATA COLLECTION

CASE REPORT FORM (CRF)

FROM SOURCE DOCUMENT TO CRF COMPLETION

Development and Evaluation of Medicinal Products, Master Degree

Student timetable between Modules A-F:

Each student will be assigned an academic tutor from the academic staff. The academic tutor will provide each student with a research project.

Each student has to work on his/her research project during the time between the teachings of Modules A to F.

EUDIPHARM ACADEMY

Leon Aarons: University of Manchester, UK

Thierry Barsalou: Product Life, F

Gerd Bode: Altanapharma, Goettingen, G

Michael Bone: ECs, UK

Jean-Pierre Boissel: Prof. Emeritus UCLB, F

François-Henri Boissel: Novapharma, F

Roselyne Boulieu: Claude Bernard University, F

Giampierro Bricca: Claude Bernard University, F

Tiphallie Ginhoux: Clinical Investigation Center (HCL), F

Catherine Brun-Strang: Sanofi-Aventis

Pierre Chatelain: Claude Bernard University, F

Patrick Chevarier: Clininfo, F

Ton Cleophas: A. Schweizer Hospital, Dordrecht, NL

Jacques Descotes: Pharmacovigilance Center (HCL), F

Ségolène Gaillard: Clinical Investigation Center (HCL), F

Erick Gaussens: Product Life, F

Pascal Girard: Inserm, F

Fouzia Guenaneche: Sanofi Pasteur MSD, Lyon,

Margaret Haugh: Sanofi Pasteur MSD, F

Jean-Marc Husson: Eudipharm, F

Judith K Jones: The Degge Group Ltd, Arlington USA

Behrouz Kassai: Claude Bernard University Lyon1, F

Sandor Kerpel-Fronius: Department of Pharmacy & Pharmacotherapy Semmelweis University, Budapest, H

Peter- Juergen Kramer: Merck Serono Research, G

Christian Laveille: Exprimo NV, H

Youssef Hidjazi: Novartis Pharma AG, Basel, CH

Alain Leizorovicz: Inserm, F

Michel Lievre: Claude Bernard University Lyon1, F

Pierre Mallia: University of Malta Medical Council

Christine Marey: Servier, F

Siavoche Mohajer: F

Lyn Morgan: Sanofi-Pasteur, F

Patrice Nony: Claude Bernard University Lyon1, F

Klaus Olejniczak: Federal Institute for Drugs and medical Devices, G

Jean- Pierre Osselaere: EPMC Pharma, Brussels, B

Yannick Pletan: Pfizer, F

Beatriz Silva Lima: University of Lisboa,

Hans Martin Spath: Claude Bernard University ISPB, F

Eric Van Ganse: Claude Bernard University, F

Thierry Vial: Center of Pharmacovigilance (HCL), F

A. Zwinderman: Academic hospital, Leiden, NL

Catherine Bertrand

Karine Van Hasbrouck

Educational objectives

1. Introduction to development of new medicines - Company input / outsourcing

Understand the development of a drug
Describe the general considerations behind the clinical development
Identify phases
Outline the steps (including “go-no go”) of a development plan for a demonstrative compound
Explain the fundamentals of quality assurance
Compile the necessary information before the first human intake
Design the calendar of the non-clinical data as a function of the clinical development program
Explain the principles of the decision of starting a development
Outline the decision making process at each main stage (first administrations to humans, phase I / II, phase III)
Formulate the objectives of phase I (human pharmacology); phase II (therapeutic exploratory), phase III (therapeutic confirmatory), phase IV studies (therapeutic use)
Apply the good clinical practice principles

2. Discovery of new medicines

Identify the strategic factors in pharmaceutical discovery and development
Formulate the problem and justify the development of a new drug
Describe the physiopathologic model
Describe the pharmacological model
Formulate a therapeutic objective
Build the therapeutic model
Explain the discovery process of a new pharmacologically active substance
Explain the high throughput screening
List the specifications of a proper animal model of disease
Explain the combinatorial chemistry
Discuss the potential outcomes of genomics and proteomics

3. Introduction to Drug Regulatory Affairs

Compare the regulatory requirements/laws for medicinal products for Human use in the main regions (Europe, Japan, USA, others)
Describe the main Medicines Agencies (EMA, FDA, MHW, HPB....)
Define the objectives of the registration process
Design the main messages in the dossier
Review the documentation for registration:

- chemical pharmaceutical
- pharmacological/toxicological
- clinical

Implement the decision making process in pre or post marketing phases

4. Toxicology and preclinical drug development

Outline good laboratory practice
Discuss an animal/in vitro model
Interpret animal and in vitro models results
Review the preclinical data
Interpret experimental toxicology data
Plan the pharmaceutical development

5. Pharmacokinetics

Define the pharmacokinetic parameters
Evaluate a pharmaceutical formulation
Assess the absorption
Identify and interpret a first pass effect
Compute a bioavailability
Assess the elimination
Evaluate a renal excretion
Evaluate a hepatic excretion
Interpret an unbound fraction
Identify time-dependent pharmacokinetics
Justify a route of administration
Compute and interpret a clearance
Compute and interpret an elimination half life
Compute and interpret a distribution volume
Distinguish linear and non-linear kinetics
Interpret a non-linear kinetics
Explain the use of compartments in pharmacokinetic modeling (physiological and descriptive)
Compute a dosing interval
Assess and evaluate a pharmacokinetic interaction
Define pharmacokinetic bioequivalence

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6. Drug metabolism

Understand drug metabolism data
Distinguish between phases I enzymes and phase II enzymes
List the cytochrome P450 family
Identify the potential consequences of genetic polymorphism on a drug metabolism
Assess ethnic differences in drug metabolism
Identify the effects of activation or inhibition of enzyme(s) on drug metabolism
Interpret data on active metabolites
Interpret in vitro prediction data
Write a review on pharmacokinetics/metabolism data

7. Pharmacodynamics

Explain the various drug action modes
Understand the mechanisms of medicinal interactions
Interpret pharmacological power
Interpret chrono-pharmacodynamics data
Evaluate structure activity relationship data
Plan the track from the pharmacologically active substance to the drug
Explain side effects mechanism
Relate data from pharmacological studies to receptor theory
Apply receptor theory to planning drug development
Explain the mechanisms of action of the drug from its pharmacological effects
Assess the relevance of an animal model
Identify the most appropriate animal/in vitro model for:
- Preclinical toxicity studies
- Preclinical metabolic exploration
Identify tachyphylaxis
Understand resistance mechanisms
Review data on rhythm in effect and/or kinetics
Write a review on pharmacological characteristics
Identify a potential for pharmacodynamic interaction

8. Population PK-PD modeling: Concentration- and dose-effect relationships (CER-DER)

Explain the fundamentals of the population approach
Assess the design of a population PK-PD study

Understand joint PK-PD modeling
Apply population approach to concentration-effect relationship estimation
Understand the model of the relation between concentration and effect at the receptor site
Interpret the value of concentration-effect parameters
Apply experimental design to the dose-effect relationship estimation
Interpret dose-effect relationship parameters
Implement biomarkers in dose-effect estimation trials

9. Medical statistics applied to clinical trial

Statistical power
Interim analysis and safety/efficacy monitoring statistical issues
Multiple statistical inferences
Stratification
Efficacy indicators
Safety indicators
Sequential statistical techniques
Equivalence testing
Definition of a hypothesis
Sample size
Sub-group analysis
Equivalence or superiority
Choice of equivalence intervals
Special features of equivalence trials
Sample size and power in equivalence trials

10. Clinical trial design

Conception of a clinical trial
Definition of healthy volunteers
Choice of outcomes
Understand the clinical trial methodology
Explain the difference between equivalence and superiority trials
Discuss the various formulations of an equivalence trial
Define the hypothesis of an equivalence trial corresponding to a given problem
Choose the comparator for an equivalence trial
Concomitant therapies
Principles of the experimental method
Principle of randomisation
Practice of randomisation
Double blind
Single blind
Fundamentals of metrology
Outcome assessment
Definition of the quality of a trial

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Principles of safety and efficacy monitoring
Wash-out period
Crossover designs
Parallel group design
Factorial designs
Stop of the study drug design
Choice of the treatment duration

11. Conduct of a clinical trial

Organising and setting up a trial
Committees
Structure of multi centre trials
Organisation of the study
Drug supply
Field trial
Selection and training of investigators
Monitoring the quality
Clinical trial audits
Data flow
Adverse event reporting
Validation of outcomes
Administrative and regulatory issues in clinical trial conduct
IRB approval

12. Clinical trial analysis and reporting

Pivotal and supportive studies
Preparing and achieving the report of a clinical trial
Data assembling
Intention to treat
Analysis according to the protocol
Groups' comparability
Sub-group analysis
Interpretation of the clinical trial results
Notion of a positive study
Notion of a conclusive study
Definition lost to follow-up
Definition of the analysis file
Database cleansing, freezing and unblinding
Definition of the intermediate, clinical and substitution criteria
The contents of the clinical trial report
Interpretation of results
Archiving of trial material
Submission of the trial report

13. Meta-analysis

Methods of efficacy and safety results synthesis
Principles and utilisation of the meta-analytic approach

Meta-analysis: statistical techniques
Regulatory concerns regarding meta-analysis
Pooled database
Extension of meta-analysis

14. Fundamentals of Pharmacoepidemiology/Pharmacovigilance

Goals of pharmacoepidemiology
Study designs in pharmacoepidemiology

15. Fundamentals of pharmacoconomics/outcome research

Principles and limitations in outcome research
Goals of pharmacoconomics
Methodology of pharmacoconomics
Parameter documentation in pharmaco-economic simulations
Define outcomes research
Describe main types of economic evaluation
Understand the methods of economic evaluation
Describe the main health care systems
Understand the different pricing systems for the drugs
Understand the role of the generic in the different healthcare systems
Understand the guidelines in different countries
Integrate the guidelines in an economic study
Understand the concept of quality of life and how to use it
Understand the different types of questionnaire
Understand how to elaborate, translate and validate a questionnaire
Understand how to choose an instrument

16. Basic information sciences

Principles of system analysis
Choose software
Choose and manage a computer service company
Fundamental notions of network
How to use computerised networks
Notions of data quality editing
Design a questionnaire
How to use a spreadsheet program
How to guarantee the security of data communication
How to promote creativity in a computer department
Modeling information
How computers work?

17. Communication

Preparing a meeting: goals, agenda, membership, setting, identification of potential problems

Running a meeting: scheduling, introduction, questions/answers, identification of problems
Minutes

Introducing and promoting a project

Presenting results

Selecting and producing presentation material

Medical writing

Publishing in scientific journals

Video conference

Meeting with Regulatory Authorities: MRFG-break out sessions, meetings with FDA

18. Bioethics

Equipoise principle

Fundamentals of ethics in research involving human subjects

Founding texts

Application to new drug clinical development

Application to clinical trial design

Ethics in protocol design

Informed consent

Ethics in monitoring, auditing and inspection of clinical trials

Ethics Committees

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Accommodation:

Residence ODALYS City Lyon Parc

Métro: Laennec



Informations/Réservations
60, avenue Rockefeller - 69008 Lyon
Tél : 04 78 77 18 18 - Fax : 04 78 77 18 17
Email : bioparc@odalyscity.com

<http://www.hotel-residence-odalys-bioparc-lyon.federal-hotel.com/>

Accès / Access

Train : A 15 mn des 2 gares TGV du centre-ville : Lyon Part Dieu et Lyon Perrache.
Liaison Transports en Commun Lyonnais :
Métro ligne D, arrêt Laennec - Tramway 2 (T2), arrêt Ambroise Paré - Bus 9, 28, 34, 38 et 79

By train: 15 minutes from the two TGV stations in the city centre: Lyon Part Dieu and Lyon Perrache.

Connections to Lyon Public Transportation:
Metro Line D: Laennec station. - Tramway 2 (T2): Ambroise Paré stop. - Buses: Numbers 9, 28, 34, 38 and 79.

En voiture : A 2 mn du périphérique Est avec accès direct aux autoroutes A6 (Paris), A7 (Marseille), A42 (Genève) et A43 (Grenoble/Chambéry/Annecy/Turin). Du périphérique Est – prendre la sortie Grange Blanche, Montplaisir, Vinatier puis suivre la direction de

Monplaisir Lyon Centre, et Hôpital Edouard Hériot par l'avenue Roosevelt puis Rockefeller. L'Hôtel-

In auto: 2 minutes from the Eastern ring road with direct access to the motorways A6 (Paris), A7 (Marseilles), A42 (Geneva) and A43

(Grenoble/Chambéry/Annecy/Turin). From the Eastern ring road, take the exit "Grange Blanche, Monplaisir, Vinatier" then follow signs to "Montplaisir Lyon Centre", and "Hôpital Edouard Hériot" on the Avenue Roosevelt then Rockefeller.

En avion : Aéroport International Lyon Saint-Exupéry (20km) et l'aéroport d'affaires Lyon-Bron (8km).

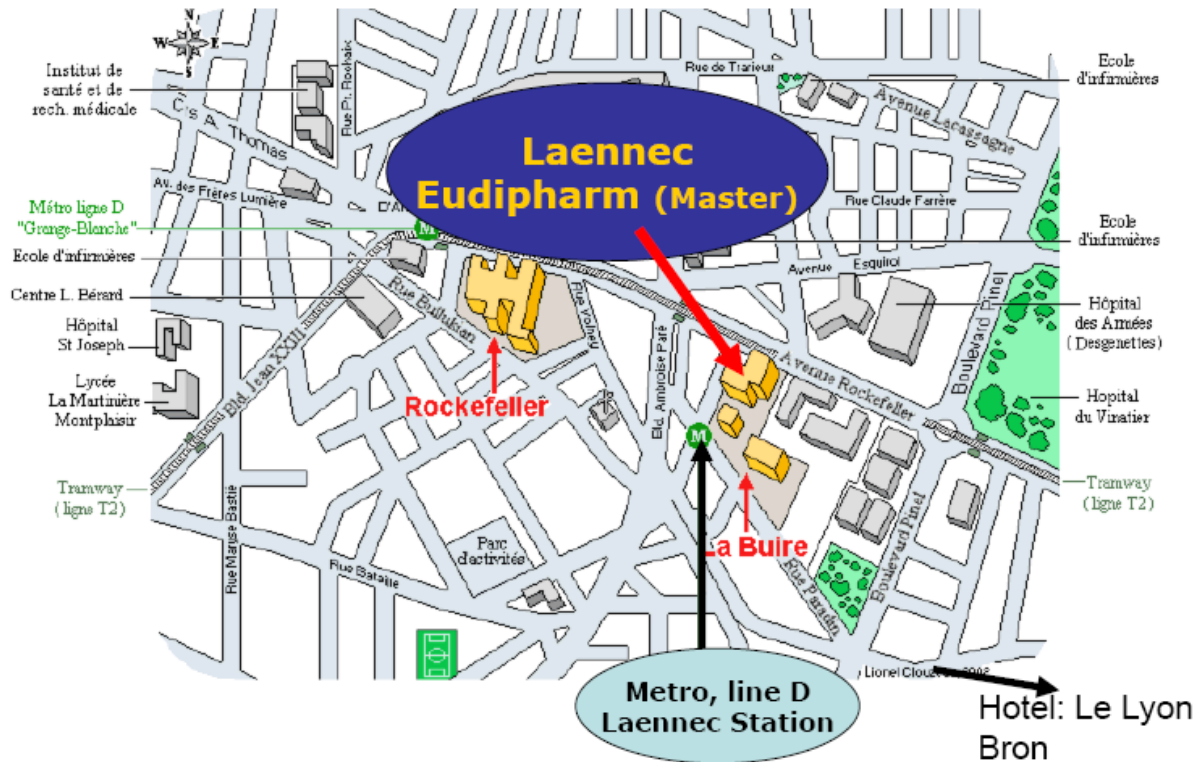
By plane: International Airport Lyon Saint-Exupéry (20km) and business aviation airport Lyon-Bron (8km).

Station Vélo'v : 150 m.

"Vélo'v" Cycle Rental Station: 150 metres.

Development and Evaluation of Medicinal Products, Master Degree

The course venue plan:



Secretariat : sc@upcl.univ-lyon1.fr - Web site : www.eudipharm.net

Phone: 0033 (0)4 78 78 57 55 (from 9 am to 12 pm)

Address : Faculté de Médecine Laennec, Service de Pharmacologie Clinique
7 Rue Guillaume Paradin 69008 Lyon, France