

## 10th – 14th Oct 2011

Base Module 2: Non-Clinical Testing,  
Pharmaceutical and Early Clinical  
Development

*Room: 105 Laennec - Mon. Oct 10*

9 a.m. – 10.30 a.m. - Klaus Olejniczak  
NON CLINICAL GUIDELINE

11 a.m. – 12 a.m. - Gerd Bode  
NON CLINICAL TESTING STRATEGY /  
IMMUNOTOXICOLOGY

1.30 p.m. – 6 p.m. - Beatriz Silva Lima  
THE NON CLINICAL DEVELOPMENT PLAN  
JUVENILE ANIMAL TESTING  
MECHANISM OF NONGENOTOXIC  
CARCINOGENS

*Room: 105 Laennec - Tues. Oct 11*

9 a.m. – 10.30 a.m. - Peter-Jürgen Kramer  
SINGLE & REPEATED DOSE TOXICITY

11 a.m. – 12 a.m. - Gerd Bode  
SAFETY PHARMACOLOGY STUDIES

1.30 p.m. – 3.30 p.m. - Peter-Jürgen Kramer  
REPRODUCTION TOXICITY

4 p.m. – 6 p.m. - Gerd Bode  
PRECLINICAL STUDIES TO SUPPORT FIRST  
HUMAN CLINICAL TRIALS

*Room: 105 Laennec - Wed. Oct 12*

9 a.m. – 10.30 a.m. - Gerd Bode  
CARCINOGENICITY

11 a.m. – 12.30 p.m. - Peter-Jürgen Kramer  
GENOTOXICITY

2 p.m. – 4 p.m. - Gerd Bode  
BIOTECHNOLOGY DERIVED PRODUCTS  
PHARMACOKINETICS / TOXICOKINETICS

4.30 p.m. – 6 p.m. - Klaus Olejniczak

LOCAL TOLERANCE / PHOTOTOXICITY  
ENVIRONMENTAL RISK ASSESSMENT

*Room: salle des theses Laennec - Thurs. Oct 13*

9 a.m. – 12 a.m. - Klaus Olejniczak  
IMPURITIES  
NONCLINICAL ANTICANCER DRUG  
DEVELOPMENT

1.30 p.m. – 2.30 p.m. - Gerd Bode  
COMMON TECHNICAL DOCUMENT (CTD)

2.30 p.m. – 3.30 p.m. - Klaus Olejniczak  
SUMMARY OF PRODUCT CHARACTERISTICS  
(SPC)

*Room: 105 Laennec - Friday. Oct 14*

9 a.m. – 11.30 a.m. – Patrice Nony  
GO NO-GO DECISIONS  
FIRST ADMINISTRATION TO PATIENTS

## 17th – 21st October 2011

INTENSIVE ENGLISH COURSE

Mon. Oct 17: 9 a.m. - 12.30 p.m. *Room : Centre  
de ressource des langues Laennec*  
& 1 p.m. – 4 p.m.

Tues. Oct 18: 9 a.m. - 12.30 p.m. *Room : Centre  
de ressource des langues Laennec*  
& 2 p.m. - 5 p.m.

Wed. Oct 19: 9 a.m. - 12.30 p.m. *Room: 1088  
Laennec*  
& 1 p.m. - 4 p.m. *Room : Centre de ressource des  
langues Laennec*

Thur. Oct 20: 9 a.m. - 12.30 p.m. *Room : Centre  
de ressource des langues Laennec*  
& 2p.m - 5 p.m. *Room : 213 Bât. J.F. Cier  
Rockefeller*

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**Fri. Oct 21: 9 a.m. - 12.30 p.m. Room : Centre de  
ressource des langues Laennec  
& 1p.m - 4 p.m**

**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. Zwiderman:** Academic hospital,  
Leiden, NL  
**Catherine Bertrand**  
**Karine Van Hasbrouck**

**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  
**Giampiero Bricca:** Claude Bernard University, F  
**Tiphalié 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 Kassaï:** 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

## Educational objectives

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### 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.

