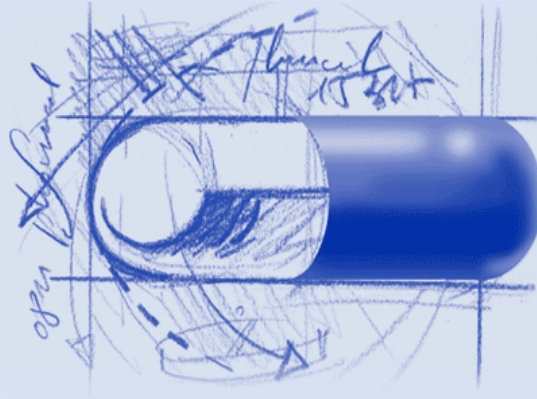


Welcome to PHARMED



ENTER

## POST-GRADUATE PROGRAMME IN PHARMACEUTICAL MEDICINE & DRUG DEVELOPMENT SCIENCES



## MODULE II Non-clinical testing, pharmaceutical and early clinical development

## **DRUG SAFETY EVALUATION: GENERAL AND REPRODUCTIVE TOXICOLOGY, MUTAGENICITY, CARCINOGENICITY, SAFETY EVALUATION OF BIOTECHNOLOGY PRODUCTS AND GENE THERAPY**

**Philippe DETILLEUX, Véronique THYBAUD, René VERLOES**

R. Verloes will review the regulatory requirements for nonclinical safety testing of pharmaceuticals, prophylactic and therapeutic vaccines. He will discuss the design and interpretation of general toxicity studies, their phasing in the drug development process and the place of toxicokinetics and of immunological readouts. A second part will address the carcinogenicity testing and the reproduction and developmental toxicity evaluation.

In vitro and in vivo tests of mutagenicity will be presented and discussed by V. Thybaud. Ph. Detilleux will consider the specific issues involved in the safety evaluation of anticancer drugs, biotechnology products and gene therapy agents.

## **CARDIAC SAFETY ASSESSMENT IN DRUG DEVELOPMENT**

**Koen VAN ROSSEM**

The course will review the scientific, regulatory and medical aspects of cardiac safety evaluation of new drug candidates. Preclinical and clinical studies to investigate prolongation of cardiac repolarization and related issues (ventricular arrhythmias) will be discussed and the applicable regulatory guidelines outlined. The importance of a scientifically sound integrated safety assessment will be illustrated.

## **DRUG DESIGN AND DEVELOPMENT**

**François DUFRASNE**

The course describes the main steps involved in drug design and development. The influence of drug stereochemistry on the biological activity, the pharmacokinetics and the metabolism and the importance of the tri-dimensional structures are discussed and illustrated.

## **DRUG FORMULATION**

**Michel FRANZ, Jonathan GOOLE**

The principal aspects of drug formulation will be discussed with special attention being paid on the early physicochemical studies performed on the active compounds. The concept of drug bioavailability will be integrated in the general trends of formulation recommended for non-conventional dosage forms taken as examples, such as oral sustained release dosage forms (single-unit *vs* multiple-unit dosage forms), transdermal forms and injectable biodegradable microspheres. The role played by *in vitro* dissolution tests and imaging techniques (gamma scintigraphy) in the development of dosage forms will be highlighted and discussed. Finally, a brief information will be given about the prospects for drug vectorisation obtained through the use of liposomes and nanoparticles.. The potential of "line extension formulations" in the framework of Life Cycle Management will be explored and several successful cases will be reviewed.

## **FROM PHARMACEUTICAL DEVELOPMENT TO PHARMACEUTICAL MANUFACTURING**

**Michel DELEERS**

This course will discuss the major issues related to industrial pharmaceutical technical development (formulations) including the manufacturing of clinical supplies, and its transfer to manufacturing with a special emphasis on quality known more now as Quality Management Systems (QMS), Quality by Design (QbD) and Process Analytical Technologies (PAT) during the development phase.

This will be presented through real examples and development cases of formulations and of product life cycle management for molecules having either reached the blockbuster status or for molecules having failed, in order to gain more insight into the reality of day to day technical development.

The course will also describe the required structures of departments in development and in manufacturing according to the cGMP guide of the US FDA and the GMP guide of EEC.

The concept of QMS and GMP in the organization, management and personnel, in the buildings, facilities and equipment, in the training programs, the validations and self-inspections, and in the control of components, containers, process and packaging will be illustrated and validation of computerized guided processes in the pharmaceutical industry will be rapidly examined (CFR21.part 11).

Finally, this course will also try to provide underpinning knowledge of the EMA and FDA agencies and inspection-operating environment for product development and manufacturing again through real examples and development cases. In this view, the concept of inspection readiness will be presented in order for pharmaceutical developers and manufacturers to be ready for cGMP & PAI (current Good Manufacturing Practice & Pre-Approval Inspections).

## **THE MOVE FROM PRE-CLINICAL TO CLINICAL STUDIES**

**Jan de HOON, Luc TRITSMANS, Luc VAN BORTEL**

Luc Tritsmans will explain the importance of accelerating the move from pre-clinical studies to clinical trials in the strategy of pharmaceutical companies. Luc Van Bortel will present and discuss the rules used to choose the dose for first in human administration (FIH). Jan de Hoon will define the following new concepts : Phase 0, microdosing, exploratory trials.



## Timetable

### Monday, November 21

- 10.00 – 12.00 *Véronique Thybaud*  
In vitro and in vivo mutagenicity studies
- 13.00 – 15.30 *Philippe Dettleux*  
Safety evaluation of anticancer drugs, biotechnology products and gene therapy agents
- 16.00 – 17.30 *René Verloes*  
Non-clinical safety evaluation (I)

### Tuesday, November 22

- 09.00 – 12.00 *René Verloes*  
Non-clinical safety evaluation (I)
- 13.00 – 15.00 *René Verloes*  
Non-clinical safety evaluation (II)
- 15.30 - 16.30 *Koen Van Rossem*  
Cardiac safety assessment in drug development

### Wednesday, November 23

- 09.00 – 12.00 *Jonathan Goole*  
Drug formulation (I)
- 13.00 – 14.30 *Michel Franz*  
Impact of drug formulation on pharmaceutical business
- 15.00 – 17.00 *François Dufrasne*  
Influence of stereochemistry on biological activity and metabolism
- 17.00 – 19.00 *Jean-Marie Boeynaems*  
Presentation and discussion of the assignment “Case study in drug development”

### Thursday, November 24

- 9.00 – 12.00 *Jonathan Goole*  
Drug formulation (II)
- 12.00 - 14.00 PHARMED LUNCH**
- 14.00 – 15.00 *Luc Tritsmans*  
Accelerating the move to clinical trials
- 15.00 – 16.30 *Jan De Hoon*  
New concepts at the boundary between preclinical and clinical research: phase 0, microdosing and exploratory trials
- 17.00 – 18.00 *Luc Van Bortel*  
How to choose the dose for first in human administration

### Friday, November 25

- 9.00 – 13.00 *Michel Deleers*  
From pharmaceutical development to pharmaceutical manufacturing

Coffee breaks : 10.30-11.00 & 15.00-15.30 (except Wednesday & Thursday )



## The Faculty

### **Jean-Marie BOEYNAEMS**

M.D., Ph.D. in biochemistry and pharmacology, Professor of pharmacology, ULB

### **Jan DE HOON**

M.D., Ph.D., M.Sc., General Manager of the Center for Clinical Pharmacology - University Hospital Gasthuisberg, Leuven; Professor of pharmacology, Faculty of Medicine and Faculty of Pharmacy, KU Leuven, Leuven, Belgium.

### **Michel DELEERS**

Ph.D., D.Sc., BA, GEO OncoBel S.A.

### **Philippe DETILLEUX**

DVM Université de Liège, Ph.D. in veterinary pathology, Iowa State University, Head Drug Safety Evaluation, Sanofi-Aventis, France

### **François DUFRASNE**

Ph.D. in pharmacy ULB, Professor at the Institute of Pharmacy of ULB and UMH

### **Michel FRANZ**

Pharmacist, University of Liège, Consultant in Pharmaceutical Product Development

### **Jonathan GOOLE**

Ph.D. in pharmacy, ULB, Lecturer at ULB

### **Véronique THYBAUD**

Ph.D. in toxicology, University of Paris, Director, Genetic Toxicology, Sanofi-Aventis, France

### **Luc TRITSMANS**

M.D., FBCPM, Senior Director, Compound Development Team Leader, Early Developments CNS, Johnson & Johnson, Belgium

### **Luc VAN BORTEL**

M.D., Ph.D., Head of Drug Research Unit Ghent (D.R.U.G.), the Phase I-II Unit of Ghent University Hospital, Belgium, Professor of Clinical Pharmacology and Therapeutics, Faculty of Medicine and Health Sciences, Ghent University, Belgium

### **Koen VAN ROSSEM**

M.D., Ph.D., Senior Director Clinical Research Stiefel Laboratories, Barrier Therapeutics, Belgium

### **René VERLOES**

M.D., Ph.D., lecturer in preclinical safety of medicines VUB, Senior Director Clinical Pharmacology & Early Development Team Leader, Tibotec



## General Information

### LANGUAGE

All courses are taught in English.

### REGISTRATION FEE

1000 Euros for the module (including access to the electronic documentation), 250 Euros for one day or 2 half-days.

Procedure: register by mail by returning a completed registration form.  
Payment should be arranged upon receipt of our bill.

### LOCATION

#### ERASME HOTEL

Route de Lennik, 790  
1070 ANDERLECHT (Brussels)  
Phone : 32-02/523 62 82  
E-mail : [info@hotelerasme.be](mailto:info@hotelerasme.be)

### HOW TO GET THE ERASME HOTEL

#### by car:

Follow the Western Ring Road (RO) and exit at « ULB, ERASME » (between exit 15 and exit 16). At the 2nd roundabout take the exit ULB, ERASME, R.S.C Anderlecht”. The hotel is on your right, 300 m after the underground station Erasme/Erasmus”

#### By underground:

Take line 5 towards « Erasme/Erasmus » and get off at the terminus. Walk through the exit 2 « Route de Lennik / Lenniksebaan ».(not Hospital Erasme). At the bottom of the stairs exit in the direction of “ Campus, ULB, ERASME”. The hotel is 300 m down the road.

### TRANSPORTATION

See our web site (venue): <http://www.ulb.ac.be/medecine/pharmed>

### REGISTRATION & INFORMATION

For more information please contact.

Mrs Bahija JELLOULI  
PHARMED – ULB CP611  
Route de Lennik, 808  
B – 1070 Bruxelles  
BELGIUM

***E-mail: [pharmed@ulb.ac.be](mailto:pharmed@ulb.ac.be)***

*Phone : 32 2 555 62 29*

*Fax : 32 2 555 62 30*