

## Academic Year 2007-2008

### sixth European Course

# Evaluation of Medicinal Products in Children

## PRELIMINARY PROGRAMME ( 49 hours)

Co-ordination : Gerard PONS, Agnes SAINT-RAYMOND, Jean-Marc HUSSON, Behrouz KASSAI, Jean-Paul LANGHENDRIES

### DAY 1 M 0

Wednesday 27 February 2008

8h00 - 8h30 : Registration / Welcome to participants

8h30 - 9h00 : Introduction to the course

- Paris V University (Rene Descartes Medical School)
- European Diploma in Pharmaceutical Medicine
- ENDIC paediatricians and pharmacologists (European Society for Developmental, Perinatal and Paediatric Pharmacology)

### DAY 1 M 1 (5h30)

Wednesday 27 February 2008

#### SPECIFIC ASPECTS OF PAEDIATRIC PHARMACOLOGY

1) 9h00 - 10h30 : **Jean-Paul Langhendries, St Vincent Hospital, Liege and UCL, Belgium (1h30).**

- Differences between adults and children : growth, development and maturation of the child.
- Impact of demographic data, prevalence of diseases and public health in children.

2) 10h30 - 11h30 : **Gerard Pons, St Vincent de Paul Hospital, Paris V University, France (1h00)**

- Extrapolability to children of side effects in adults.
- Potential long term side effects of drugs related to exposure during growth and maturation.

11h30 - 12h00 BREAK

3) 12h00 - 13h00 : **Kalle Hoppu, Helsinki University, Helsinki, Finland (1h00) TBC**

- Main diseases unique to children requiring a specific drug evaluation.

13h00 - 14h00 LUNCH

4) 14h00 - 15h00 : **Evelyne Jacqz-Aigrain, Robert Debre Hospital, Paris, France (1h00)**

- Prospects of pharmacogenomics in paediatric pharmacology.

5) 15h00 - 16h00 : **Anders Rane, Karolinska Institute at Karolinska University, Sweden (1h00)**

- Pharmacokinetics and pharmacodynamics (PK/PD) changes in children during maturation and diseases

1) 9h00 - 10h00 : Imti Choonara/**Sharon Conroy, Nottingham University, Derby, UK (1h00) TBC**

- Extent of unlicensed and off-label use of medicinal products in children.

2) 10h00 - 11h00 : **Tony Nunn, Royal Liverpool Children's NHS Trust, Liverpool, UK (1h00)**

- The needs for pharmaceutical forms of medicinal products adapted to children.

**11h00 - 11h30 BREAK**

3) 11h30 - 12h30 : **Dirk Mentzer, Paul Ehrlich Institute, Langen, Germany (1h00)**

- Manage the specific aspects of pharmacovigilance in children.

**12h30 - 13h30 LUNCH**

4) 13h30 - 14h30 : **François Hirsch, Eur. Commission Research Directorate, Brussels, Belgium (1h00)**

- Specific ethical issues concerning clinical trials in children including the use of placebo and obtention of consent form.
- Main cultural differences within Europe.

5) 14h30 - 15h30 **Daniel Brasseur, EMEA/CPMP, London, U.K. (1h00)**

- The Implementation of the Paediatric Regulation. Tasks and Mandates of the different parties

**15h30 - 16h00 BREAK**

6) 16h00 - 17h30 : **Agnes Saint-Raymond, EMEA, London, UK (1h30)**

- Ethical, regulatory and legal framework of the drug development in children.

1) 8h30 - 9h30 : **Gerard Pons, St Vincent de Paul Hospital, Paris V University, France** (1h00)

- Explain and implement the methodological and technical specifications of clinical trials in children, including placebo effect, choice and assessment of good endpoints.

2) 9h30 - 10h30 : **Jean-Louis Steimer, Novartis Pharma, Basel, Switzerland** (1h00)

- Place of pharmacokinetics and pharmacodynamics modelling in drug development in children. Examples

**10h30 - 11h00 BREAK**

3) 11h30 – 12h30 : **Amin Rostami-Hodjegan, Royal Hallamshire Hospital, Sheffield, U.K.** (1h00) **TBC**

- Modelling of the influence of growth and maturation in drug development in children. Example of the maturation of drug metabolism.

**12h30 - 13h30 LUNCH**

4) 13h30 – 14h30 : **Martin Posch, Medical University, Vienna, Austria** (1h00) **TBC**

- Place of sequential methodological approaches in phase 1-2 clinical studies during drug development in children.

5) 14h30 – 15h30 : **John Whitehead, University of Reading, U.K.**(1h00) **TBC**

- Place of sequential methodological approaches in phase 3 clinical studies during drug development in children.

**15h30 - 16h00 BREAK**

6) 16h00 – 17h00 : **Behrouz Kassai, Laënnec University, Lyon, France** (1h00)

- Clinical cases : meta-analysis in paediatrics.

7) 17h00 – 18h00 : **Lucien Abenheim, London School of Epidemiology, London, U.K.** (1h00) **TBC**

- Specific methodological aspects in pharmaco-epidemiology in children.

1) 8h30 - 9h30 : **Beatriz Silva-Lima, Lisbon University, Portugal & EMEA, CPMP/Safety WP, UK (1h00)**

- Required preclinical studies for the marketing authorization of a new medicinal product to be used in children (including juvenile animal models) : the authorities viewpoint.
- Preclinical studies for a new drug application in children : industry strategy

2) 9h30 - 10h30 : **Kerstin Westermark, Medical Products Agency, Uppsala, Sweden (1h00)**

- Rare diseases, orphan drug and how to develop an orphan drug : academic and EMEA/COMP viewpoints.
- Methodology of CTs in MDD for orphan drugs : experience of COMP

**10h30 - 11h00 BREAK**

3) 11h00 - 12h30 : **Nathalie Seigneuret, EMEA, London, UK (1h30)**

- Paediatric Investigation Plan
- Reasons to initiate drug development in children at different phases of drug development in adults : the regulatory (EMEA/CPMP) viewpoint (scientific advice...)

4) 12h30 - 13h30 : **Khazal Paradis, Genzyme Europe, Naarden, The Netherlands (1h00)**

- Rationale, barriers and opportunities for developing a paediatric medicine : a research based pharmaceutical industry approach.

1) 8h30 - 10h00 : **Sandra Kweder, FDA, Washington, U.S.A.** (1h30) **TBC**

- Drug evaluation by Regulatory Authorities and specific issues linked to their use during pregnancy : product information/labeling.
- Questioning clinical trials on medicinal products possible during pregnancy

2) 10h00 – 11h00 : **Donald Mattison, National Institute of Child Health and Human Development, Rockville MD, USA** (1h00)

- Principles and methodological issues on the evaluation of placental drug transfer.

**11h00 - 11h30 BREAK**

3) 11h30 - 12h30 : **TBF FDA** (1h00)

- Mathematical model of transplacental transfer of drugs : the example of retinoids.
- PB-PK model for transfer of drugs into breast milk.

**12h30 - 13h30 LUNCH**

4) 13h30 - 15h00 : **Michael D. Reed, Rainbow Babies & Children's Hospital, Cleveland, U.S.A.** (1h30)

- Different clinical situations related to fetal drug therapy. Methodological issues on drug evaluation in these situations and available evidence-based data. (1h00)
- **Case study** (30 min)

5) 15h00 - 16h00 : **Elisabeth Elefant, Trousseau Hospital, Paris, France** (1h00)

- Drug therapy in pregnant women.
- Risk of drug exposure at different stages of pregnancy : consequences for drug use in pregnant women.

**16h00 - 16h30 BREAK**

6) 16h30 - 18h00 : Moderator **Elisabeth Elefant, Trousseau Hospital, Paris, France** (1h30)

Panel discussion with : **Jean-Marc Husson, Sandra Kweder, Donald Mattison, Gerard Pons, Michael D. Reed.**

**Case studies** : 3 cases / 6 groups :

- **Case 1** : Drug exposure during early pregnancy
- **Case 2** : Drug exposure during late pregnancy
- **Case 3** : Drug exposure during before delivery

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**DAY 6 M 6 (7h45)**

**Thursday 27 March 2008**

**DRUG EVALUATION IN VARIOUS SPECIFIC THERAPEUTIC AREAS IN CHILDREN.  
STATE OF THE ART. PROTOCOL DESIGN (WORKSHOP)**

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1) 8h30 – 10h30 : **Marie-Claude Bonnet, Sanofi-Pasteur, Lyon, France** (2h00) **TBC**

Practical training on the design of one specific protocol with its CRF in a therapeutic area : (lecture)

- **Position of the specific problem** : state of the art through evidence based medicine on drug evaluation in vaccinations in children.
- **Identification of all ethical, methodological, regulatory issues** relevant to the design of the study protocol/CRF.

**10h30 - 11h00 BREAK**

2) 11h00 - 12h30 : **Marie-Claude Bonnet, Sanofi-Pasteur, Lyon, France** (1h30)

- Practical training on the design of one specific protocol with its CRF (instructions);

**12h30 - 13h30 LUNCH**

3) 13h30 - 15h00 : Co-ordination by **Marie-Claude Bonnet, Gerard Pons and Jean-Marc Husson** (1h30)

- Drafting the protocol and the CRF by students in 3 working groups

**15h00 - 15h30 BREAK**

4) 15h30 - 18h15 : Co-ordination by **Marie-Claude Bonnet, Gerard Pons and Jean-Marc Husson** (2h45)

- Drafting the protocol and the CRF by students in 3 working groups

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**DAY 7 M 6 (1h30)**

**Friday 28 March 2008**

**DRUG EVALUATION IN VARIOUS SPECIFIC THERAPEUTIC AREAS. STATE OF THE ART.  
PROTOCOL DESIGN (WORKSHOP CONTINUED...)**

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1) 8h30 - 10h00 : Co-ordination by **Jean-Marc Husson and Gerard Pons** (1h30)

- Reports by the 3 different student working groups

**10h00 - 10h30 BREAK**

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**DAY 7 M 7 (6h00)**

**Friday 28 March 2008**

**DRUG EVALUATION IN A SPECIFIC THERAPEUTIC AREA IN CHILDREN. STATE OF THE ART.**

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2) 10h30 - 12h00: **Fred Zepp, Johannes Gutenberg University, Mainz, Germany** (1h30) **TBC**

- Lessons from the experience of the German Paediatric Network (PaedNet), on the basis of one specific clinical study.

3) 12h00 - 13h30 : **Hidefumi Nakamura, National Children's Medical Center, Tokyo, Japan** (1h30)

- Lessons from the experience of the Japanese Paediatric Network.

**13h30 – 14h30 LUNCH**

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4) 14h30 - 16h00 **Bart van Overmeire, Antwerpen University Hospital, Belgium** (1h30)

- Specific aspects of drug evaluation in ductus arteriosus in neonates

5) 16h00 - 17h30 : **Catherine Chiron, Necker Hospital, Paris, France** (1h30 mn)

- Specific aspects of the evaluation of epilepsy in children, differences with adults.

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**DAY 8 M 7 (3h15)**

**Saturday 29 March 2008**

**DRUG EVALUATION IN A SPECIFIC THERAPEUTIC AREA IN CHILDREN. STATE OF THE ART.**

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1) 8h30 - 10h00 : **Gilles Vassal, Gustave Roussy Institute, Villejuif, France** (1h30)

- Specific aspects of the evaluation of drugs in cancer diseases in children.

2) 10h00 - 11h30 : **Chantal Wood, Robert Debre Hospital, Paris, France** (1h30)

- Specific aspects of the evaluation of pain in children, differences with adults

3) 11h30 - 11h45 : Conclusions of the meeting : **Jean-Marc Husson, Gerard Pons** (15mn).