

# Module 7: Non-clinical Development and Documentation

**February 29 – March 2, 2012**  
**Medicademy, Lersoe Park Allé 101,**  
**2100 Copenhagen, Denmark**

**Course Leaders:** *Jens Thing Mortensen*, DVM, DABT, European Registered Toxicologist  
Principal Senior Scientist  
LAB Research (Scantox), Denmark

*Peter Ravn Brinck*, Director, Tox and Safety Pham at Novo Nordisk A/S,  
Denmark

## **DAY 1**      **Wednesday February 29, 2012**

**08.30 – 9.15**      **Introduction**  
*Medicademy/Course leaders*

**09.15 – 10.00**      **CTD: Overview of Pharmacology, Pharmacokinetics and Toxicology**

- How to build up the non-clinical development plan to comply with CTD module 4 requirements
- Structure of the CTD module
- Comparison between previous application formats and the CTD format incl. module 2

*Dr. Gerd Bode, FACP, PhD, Consultant, Germany, lecturer at the Universities of Goettingen, Bonn and Essen, in Germany, and at the University of Lyon in France*

**10.00 – 10.15**      **Coffee/tea**

**10.15 – 11.00**      **Timing of Non-Clinical Studies**

- What is needed for Phase I, Phase II and Phase III studies?
- What is needed for approval
- ICH M3 with a special focus on regional differences

*Allan Dahl Rasmussen. H. Lundbeck A/S, Denmark*

**11.00 – 12.00 Pharmacology**

- Primary pharmacodynamics
- Secondary pharmacodynamics
- Safety pharmacology (ICH S7)
- Pharmacodynamic drug interactions

*Dr. Gerd Bode, FACP, PhD, Consultant, Germany, lecturer at the Universities of Goettingen, Bonn and Essen, in Germany, and at the University of Lyon in France*

**12.00 – 13.00 Lunch**

**13.00 – 14.00 Pharmacokinetics**

- ADME
  - Which studies are needed?
  - Analytical methods and validation
- Pharmacokinetic drug interaction (non-clinical)
- Other pharmacokinetic studies
- ICH S3

*Lena Alifrangis, Senior Scientist, Development DMPK, Novo Nordisk A/S, Denmark*

**14.00 – 14.45 General Toxicity Studies, incl. immunotoxicity**

- CPMP/SWP/1042/99, ICH S4
- Single and repeat dose toxicity studies
- Dose response
- NOAEL, MTD
- Target organs
- Administration routes
- Duration of studies
- Reversibility

*Allan Dahl Rasmussen. H. Lundbeck A/S, Denmark*

**14.45 – 15.00 Coffee/tea**

**15.00 – 15.45 Genotoxicity**

- ICH S2
- Core battery of tests
- Follow-up tests
- Go/no-go decisions

*David Tweats, Genetic Toxicology Consultant, UK*

**15.45 – 16.30 Local Tolerance and Other studies**

- Local tolerance (CPMP/SWP/2145/00)
- Allergy
- Photo Toxicity

*Jørgen Schützsack, Senior Toxicologist, LEO Pharma, Denmark*

<b>16.30 – 16.45</b>	<b>Coffee/tea/sandwich</b>
<b>16.45 – 18.45</b>	<b>Workshop Day 1</b> <i>Course Leaders</i>
<b>19.15</b>	<b>Networking Dinner at Hotel Twentyseven in Copenhagen</b>

**DAY 2 Thursday March 1, 2012**

**08.30 – 08.45**      **Short Summary of Day 1 and Introduction to Day 2**  
*Course Leaders*

**08.45 – 09.30**      **Application for First in Man**

- EMA procedures
- FDA procedures

*Ann Christine Korsgaard, Genmab A/S, Denmark*

**09.30 – 10.15**      **Interaction with Clinical (CTD Module 5)**

- Indication (kinetics, tolerance and efficacy)
- Population (healthy, patients, sex, age and other medication)
- Posology
- Trial Design (“First in Man”)

*Lars Iversen, Senior non-clinical project manager, Novo Nordisk A/S, Denmark*

**10.15 – 10.30**      **Coffee/tea**

**10.30 – 11.15**      **Interaction with Quality (CTD Module 3)**

- Test substance from Lab-scale to production
- Specification in relation to:
  - Impurities
  - Degradation products
  - (ICH Q3)
- Special requirements to non-clinical formulation, e.g. dose, concentrations, and stability
- Analysis
- Biological samples

*Henry Stemplevski, Pharmacotoxicologist and Preclinical Assessor, MHRA, The United Kingdom*

**10.15 – 11.30**      **Coffee/tea**

**11.30 – 12.30**      **Reproduction**

- Reproduction (ICH S5)

*Graham Bailey, Janssen Pharmaceuticals (J&J), Belgium*

**12.30 – 13.30**      **Lunch**

**13.30 – 14.00**      **Juvenile Toxicity**

- Juvenile – toxicity

*Graham Bailey, Janssen Pharmaceuticals (J&J), Belgium*

- 14.00 – 14.45      Carcinogenicity**
- Carcinogenicity (ICH S1)
- Andrew Makin, LAB Research (Scantox), Denmark*
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- 14.45 – 15.00      Coffee/tea**
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- 15.00 – 16.00      Biotechnology Products**
- ICH S6
  - Classification of biotech products
  - Differences between non-clinical programs for small molecules and biotech products
  - Risk assessment and regulatory aspects of biotech products
- Vibeke Miller Breinholt, Genmab, Denmark*
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- 16.00 – 16.15      Coffee/tea/sandwiches**
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- 16.15 – 18.15      Workshop Day 2**  
**- coffee/tea and sandwiches included**
- Course Leaders*
- 18.15 – 18.30      Presentation of Group Work for Day 3**

**DAY 3      Friday March 2, 2012**

**08.30 – 08.45      Short Summary of Day 2 and Introduction to Day 3**  
*Course Leaders*

**08.45 – 09.45      Life Cycle Management**

- New Indications
- Line Extensions
- Fixed Combinations
- Excipients
- Examples

*Tina Zinck, Non-clinical Assessor, Ph.D., Danish Medicines Agency, Denmark*

**09.45 – 10.15      Implications of non-clinical findings for the EU and FDA labelling text**

- Information, which is always included
- Other information
- Differences between EU and FDA

*Paul Baldrick, Head, Regulatory Affairs for Pharmaceuticals within the Consultancy and Regulatory Services Department at Covance-Harrogate, UK*

**10.15 – 10.30      Coffee/tea**

**10.30 – 11.30      Risk Assessment – Regulatory Body View**

- The assessment report

*David Jones, BSc, MSc, EurBiol, CBiol, MIBiol, Registered Toxicologist, MHRA, UK*

**11.30 – 12.15      Risk Assessment – Industry View**

*Paul Baldrick, Head, Regulatory Affairs for Pharmaceuticals within the Consultancy and Regulatory Services Department at Covance-Harrogate, UK*

**12.15 – 12.30      Risk Assessment – Discussion and rounding-off**

*Paul Baldrick, Head, Regulatory Affairs for Pharmaceuticals within the Consultancy and Regulatory Services Department at Covance-Harrogate, UK*

*David Jones, BSc, MSc, EurBiol, CBiol, MIBiol, Registered Toxicologist, MHRA, UK*

**12.30 – 13.15      Lunch**

**13.15 – 15.30      Workshop: Toxicology**  
*Course Leaders*

**15.30 – 16.15      Summary of the Non-Clinical Module**  
*Course Leaders and Participants*