DRUG INFORMATION ASSOCIATION

Dedicated to Your Information & Advancement

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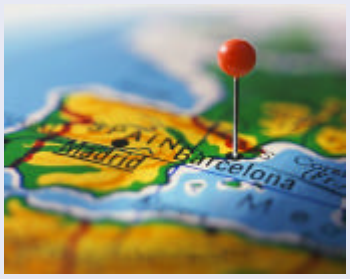
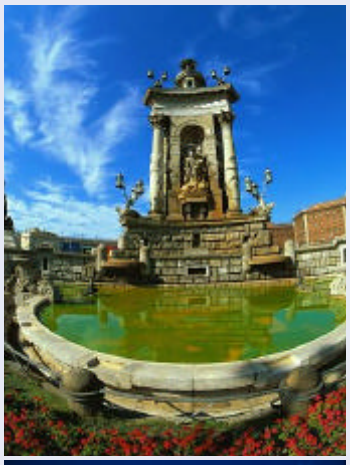
September 26-27, 2002 - Hotel Fira Palace, Barcelona, Spain





3rd International Workshop on Statistical Methodology in Non-Clinical R&D

Programme Chairperson

Dr. Bruno Boulanger, Eli Lilly, Belgium

Programme Committee

Prof. Ludwig Hothorn, University of Hanover, Germany

Prof. Geert Molenberghs, Limburgs University Center, Belgium

Magnus Astrand, AstraZeneca, Sweden

Prof. David Stephens, Imperial College, UK

Workshop Objectives

The goal of the workshop is to bring together Statisticians and other professionals dealing with applied statistics in the non-clinical area, from the Pharmaceutical Industry, Academia and Regulatory Agencies, to provide an Open Forum to discuss the following topics:

- Important issues of current interest to applied statistics in the non-clinical research and development.
- The challenges the non-clinical statisticians will face tomorrow with the implementation of new technologies in the pharmaceutical research process.
- How could statisticians impact the new challenges of speed and quality that the pharmaceutical discovery should overcome?
- The contribution of statisticians in the future of "in silico" technologies in discovery.
- Appropriate statistical methods for the area (as described in non-clinical guidelines).

Key Topics

- High-throughput screening
- Analyses of Metabonomics & Proteomics assays
- DNAμ - Arrays
- Bioinformatics
- Modelling in Non-Clinical R&D
- Repeated measures in in-vivo studies
- Development and Validation of Bioassay
- Pharmacological studies
- Formulation optimization
- Multicriteria Decision Methods
- Molecular Diversity
- Optimal designs
- Statistics for Quantitive Structure Activity Relationship (SAR)

About the Drug Information Association

With more than 27,000 members worldwide, the Drug Information Association (DIA) is the premier member-driven organization encompassing the full continuum of disciplines in the pharmaceutical and related industries. The mission of DIA is to serve and develop members by providing a neutral, global forum that promotes the exchange of information critical to their professional performance and achievement. The goal of DIA is to be the most effective means for members to obtain the knowledge they need to advance their career, their profession, and their organization.

Wednesday, September 25, 2002

18:00-19:00 Registration

Thursday, September 26, 2002

08:00 Registration

08:45 Welcome Address by the Chairperson
BRUNO BOULANGER, ELI LILLY, BELGIUM

09:00 Session 1

SAFETY ASSESSMENT
Session Chairperson:
Prof. Ludwig Hothorn, University of Hannover, Germany

Two-Stage Testing on Safety: A Statistical View
Dr. Dieter Hauschke, Altana Pharma, Germany
- Proof of safety versus proof of hazard
- Two-stage adaptive analysis based on the ratio of location parameters
- Determination of the maximum safe dose
- Demonstration of the proposed procedure in a real mutagenicity assay

Immuntoxicological Assays: Measuring and Reducing the Variability
Graham Healey, Huntingdon Life Sciences, UK
- Analysis of historical data to assess variability sources
- Optimisation of randomisation and replication
- Scheduling of experimental work in a production environment

10:30 Coffee Break

11:00 Session 2

SPECIAL CASES IN PHARMACOLOGY
Session Chairperson:
Ludwig Hothorn, University of Hannover, Germany

Cox's Proportional Hazards Model with Frailties: An Application to Repeated Functional Assessment after Transient Middle Cerebral Artery Occlusion in the Rat
Andrew Llyod, GlaxoSmithKline Pharmaceuticals, United Kingdom
- Overview of scientific method
- Issues in analysis of response
- Frailty model used in analysis

Statistical Analysis of Electroencephalograms
Céline Bugli, Université Catholique de Louvain-la-Neuve, Belgium
- Cleaning data using Independant Component Analysis (ICA)
- ICA to reduce the problem dimension

Inference: detection of treatment effect

12:30 Lunch

14:00 Session 3

DESIGNS FOR PHARMACOLOGY
Session Chairperson:
Dr. Bruno Boulanger, Lilly Development Centre, Belgium

Non-Sequential Optimal Designs for some Michaelis-Menten and Emax Models
Carl-Fredrik Burman, AstraZeneca R&D, Sweden
- Local optimal design solutions
- Bayesian optimal design
- Practical problems when applying the theory

Optimal Designs to Maximise Inverse Prediction Precision in Calibration Problems - Application to the Linear Model and to the Four Parameters Logistic Curve (4-PL)
Nancy Francois, Université Catholique de Louvain-la-Neuve, Belgium
- Inverse prediction in calibration problems
- Optimal designs: linear and 4PL models
- Comparison with equally-spaced designs

Towards an Optimised Management of Pharmacological Data
Corinne Haimez, Institut de Recherche Servier, France
- Introduction about the characteristics of non-clinical experimental protocols
- Solution proposed to our researchers to store and analyse their data
- Conclusions about the benefits of such an approach

15:30 Coffee Break

16:00 Session 4

LIBRARY DESIGN
Session Chairperson:
Bruno Boulanger, Lilly Development Centre, Belgium

A Fast Exchange Algorithm for Designing Focused Libraries in Lead Optimisation
Céline Le Bailly de Tilleghem, Université Catholique de Louvain-la-Neuve, Belgium
- Objectives of focused library design
- Our algorithm
- Comparison with other existing methods

A Density-Based Criterion for Optimal Molecular Diversity Sampling in Drug Design
Christelle Darstein, Eli Lilly & Company, USA
- High Throughput Screening (HTS): unrealisable to screen all compounds
- Smart sampling: diversity, easy to synhesize
- Sampling in high-density areas

17:00 Reception

Friday, September 27, 2002

09:00 Session 5

ANALYSES IN PHARMACOLOGY
Session Chairperson:
Magnus Astrand, AstraZeneca R&D, Sweden

Design and Analysis of Pharmacological Studies in Osteoporosis
Ludwig Hothorn, University of Hannover, Germany
- Proof of efficacy and equivalence
- A priori power of a multi-arm study
- Multiple endpoints

Choice of the Statistical Methodology and the Use of Interim Analyses in Pharmacological Studies
Simon Hitier, Pfizer Global R&D, France
- How to improve the choice of the statisticial methodology
- Why and when should we use interim analyses in pharmacological studies?

10:30 Coffee Break

11:00 Session 5 (Continued)

Analysis of Dose-Response Curves by a Semi-Parametric Approach
Benoît Beck, Lilly Services S.A., Belgium

European Regulatory Guidance for the Statistical Analysis of Non-Clinical Areas
Joachim Röhmel, Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM), Germany
- Dissolution tests
- Biological assays
- Problems in toxicology

12:30 Lunch

14:00 Session 6

GENOMICS
Session Chairperson:
David A. Stephens, Imperial College School of Medicine, UK

Exploration of Gene Expression Data by Spectral Map Analysis
Luc Wouters, Janssen Pharmaceutica N.V., Belgium
- Overview of multivariate projection methods
- Introducing weighted spectral map analysis
- Application to microarray data

Analysis of a DNA Microarray Experiment
Linda Robb, GlaxoSmithKline Medicines Research Centre, UK
- A description of the design and science of the DNA mircroarray experiment
- An explanation of the main analyses used
- The interpretation of the final discrimant model

15:15 Coffee Break

15:30 Session 6 (Continued)

Bayesian Methods in the Analysis of Differential Expression
David A. Stephens, Imperial College School of Medicine, UK
- Statistical analysis of microarray data
- Bayesian methods for assessing differential expression
- Bayesian gene clustering
- Gene selection using Markov Chain Monte Carlo (MCMC) and probabilistic rule-based methods

Low-Level Analysis of Oligonucleotide Arrays: Normalisation and Expression Indices
Magnus Astrand, AstraZeneca R&D, Sweden

16:30 End of the Workshop

Hotel & Travel Information

The DIA has blocked a limited number of rooms at the:
Fira Palace Hotel
Avda. Rius i Taulet, 1-3
08004Barcelona, Spain

at the special rate of:
Double Standard Room: Euro 205.-
Double for Single Occupancy Standard Room: Euro 180.-
(rates are inclusive of Buffet Breakfast, Service Charges, excluding 7% VAT)

Attendees must make their own hotel reservation by telephone: +34 93 426 22 23 or fax: +34 93 425 50 47
or e-mail: reception@fira-palace.com referring to the DIA Workshop.

A deposit payment for one night must be made to secure the reservation by providing, with signature, the name, number and expiry date of your credit card.

IMPORTANT: To be assured of accommodation in Barcelona, the registrants are recommended to complete their reservation, if possible, by August 14, 2002.

Barcelona, the capital of Catalonia, is located on the coast and bounded by the Collserola ridge and rivers Besós and Llobregat. The city is less than 150 kilometres fromthe Pyrenees. Barcelona's location on the shores of the Mediterranean means that it enjoys a warm, welcoming climate and pleasant temperatures all year round.

Barcelona's location on the shores of the Mediterranean, near to France and the rest of Europe, means that it is well-served by transport links and is accessible by land, sea and air. The city has a number of railway stations and a rail network providing connections with the rest of Spain and a number of European cities.

Workshop Cancellation Policy

On or before **September 21, 2002**
An administrative fee will be deducted from the registration fee:
Member and Nonmember = EURO 200.-
Government & Academia (Member/Nonmember) = EURO 100.-

Registrants who do not cancel by the date above and do not attend, will be responsible for the full registration fee. Registrants are responsible for cancelling their own hotel reservations. Cancellations must be in writing. You may transfer your registration to a colleague at any time. Please notify DIA of any such substitutions as soon as possible. DIA reserves the right to alter the venue, if necessary. If an event is cancelled, DIA is not responsible for airfare, hotel or other costs incurred by registrants.