

E 15 10



Drug Information Association

The Leading Member-Driven,  
Multi-Disciplinary, Non-Profit Association

September 14-15, 2000  
Hotel Royal Plaza Inter-Continental  
MONTREUX, Switzerland



# 2nd International Workshop on: Statistical Methodology in Non-Clinical R&D

## Programme Chairperson

Dr. Merete JØRGENSEN, Novo Nordisk A/S, Denmark, Member of EFSPi

## Programme Committee

Dr. Bruno BOULANGER, Lilly Development Centre, Belgium

Dr. Dennis LENDREM, TTC Consultants, UK

Prof. Ludwig HOTHORN, University of Hannover, Germany

Dr. Tomas MORSING, Astra Zeneca AB, Sweden

Dr. Yves-Laurent GRIZE, AICOS Technologies AG, Switzerland

## Workshop Objectives

The goal of the workshop is to bring together statisticians and others dealing with applied statistics in the non-clinical area, from the pharmaceutical industry, academia and regulatory agencies, to provide an open forum to discuss:

- Important issues of current interest to applied statistics in the non-clinical research and development.
- Appropriate statistical methods for the area and to be described in non-clinical guidelines, primarily from FDA and ICH.

The various sessions will allow sufficient time for fruitful discussions and sharing experiences between speakers and participants.

## Key Topics

Topics for the programme are statistical issues in relation to the areas:

- High Throughput Screening
- Pharmacology
- Discovery
- Stability and Specifications
- Applications of Experimental Designs
- Bioassay

## Who Should Attend?

The target group for this meeting are people with interest in statistical issues in relation to pre- and non-clinical R&D activities. These cover both drug discovery, analytical and documentation issues. Statisticians as well as non-statisticians working in these fields in pharmaceutical industry, academia, contract research organisations or at regulatory authorities are encouraged to participate.

Additional information will be progressively available  
on the DIA Home Page [www.diahome.org](http://www.diahome.org)

**2nd International Workshop on:  
Statistical Methodology in Non-Clinical R&D**

# PROGRAM

Wednesday, September 13, 2000

18:00 Registration

## Thursday, September 14, 2000

08:00 Registration

09:00 Session 1

### HIGH THROUGHPUT SCREENING

Session Chairperson:

Dr. Yves-Laurent Grize, AICOS Technologies AG, Switzerland

### Recent Biostatistical Aspects of Design and Analysis of HTS

Prof. Ludwig Hothorn, University of Hannover, Germany

- \* Microfiber assay: new design to avoid between and within plate bias
- \* Estimation of false-positive and false-negative decision rates
- \* Strategies for hit definition

### HTS - Does a Statistical Solution Exist?

Dr. Frank Bretz, University of Hannover, Germany

- \* Discussion of statistical aspects
- \* Application of the Wilcoxon rank sum test
- \* Strategies for detecting statistically significant hits

10:30 Coffee Break

11:00 Session 1 (Cont'd)

### Molecular Diversity: Statistical Perspectives and Approaches

Dr. David Cummins, Eli Lilly & Company, USA

- \* Diversity analysis: definition, settings and goals
- \* Review and development of new methods
- \* Comparison of methods using Monte Carlo simulation

12:30 Luncheon

14:00 Session 2

### DISCOVERY

Session Chairperson:

Dr. Tomas Morsing, AstraZeneca, Sweden

### Stochastic Process Models for Structure-Activity Relationships

Dr. Markus Abt, F. Hoffmann-La Roche Ltd., Switzerland

- \* Discussion of structure activity relationships
- \* Presentation of Gaussian Stochastic Process Models as a flexible tool allowing for non-linearities as well as interactions
- \* Application of the methodology to QSAR data sets and comparison with alternative methods

### Statistical Software Solutions for Discovery's Problems

Dr. Katrina Todd, Pfizer Central Research, United Kingdom

- \* To describe our solution to our scientist's problem
- \* To indicate the breadth of our software
- \* To outline the benefits of developing our own software

### Analysis of Gene Expression Data

Dr. Per Broberg, AstraZeneca R&D Lund, Sweden

- \* Brief introduction to microarrays as a datasource
- \* Description of the questions people try to answer
- \* Share experience of some analysis approaches based on multivariate and time series analysis

15:30 Coffee Break

16:00 Session 3

### PHARMACOLOGY

Session Chairperson:

Prof. Ludwig Hothorn, University Hannover, Germany

### When Not to Use Repeated Measures ANOVA: Two Case Studies in Pharmacology

Dr. Dennis Chanter, Quintiles, United Kingdom

- \* How to extract biologically useful information from an analysis
- \* Example 1: The isolated guinea pig ileum assay
- \* Example 2: The Morris water maze study

### Statistical Methods for Determining Synergism or Antagonism from Response Surface Experiments

Dr. Gerald Hajian, Schering Plough Research Institute, USA

- \* Review parametric response surface methods
- \* Show spatial regression models (semi-parametric)
- \* Show thin plate spline models (non-parametric)

17:30 Reception

19:00 Departure for Social Event

## Friday, September 15, 2000

Session 4

### BIOASSAY

Session Chairperson:

Dr. Bruno Boulanger, Lilly Development Centre, Belgium

### Immunological Assays: Establishing a Basis for Routine Analysis and Curve-Fitting

Mr. Graham Healey, Huntingdon Life Sciences, United Kingdom

- \* To provide a classification for the many immunological assays used in R&D
- \* To provide the biological background and common basis for assays
- \* To explore the link between the biology and the statistical analysis

### Comparison of Maximum Likelihood and Simplified Method for Titer Estimation in Dilution Assays

Dr. René Tabanera, Novo Nordisk A/S, Denmark

- \* Example of TCIDSO calculation for the vaccinia virus
- \* Comparison of maximum likelihood method and two simplified methods based on the example
- \* Evaluation of the three methods based on simulated data

### Calibration Precision Profiles in Assay Optimization

Dr. Viswanath Devanarayan, Eli Lilly & Company, USA

- \* Review of the relationship between calibration precision and assay performance
- \* Describe methods for using precision profile parameters to the calibration curve
- \* Demonstrate the advantages of these methods for optimizing pharmaceutical assay

Coffee Break

Session 5

### STABILITY AND SPECIFICATIONS

Session Chairperson:

Dr. Merete Jørgensen, Novo Nordisk A/S, Denmark

### Shelf Life Estimation for Stability Studies

Mr. Claes Ekman, AstraZeneca, Sweden

- \* Random batch approach vs. the FDA recommendation
- \* ML vs. REML in the random batch approach

### On the Use of Stability Data to Determine Internal Release Limits by Allen's Formula - A Case Study

Dr. Jørgen Iwersen, Novo Nordisk A/S, Denmark

### Quality Control Sample Sizing Using A Bayesian Approach

Ms. Janice Freeburn, Pfizer Central Research, United Kingdom

- \* General discussion of sample size determination
- \* Show how prior knowledge can be incorporated
- \* An easy to use graphical tool

Luncheon

Session 6

### APPLICATIONS OF EXPERIMENTAL DESIGNS

Session Chairperson:

Dr. Dennis Lendrem, TTC Consultants, United Kingdom

### Fractional Factorial Designs for Process Parameter Setting: Is Preventing Their Widespread Use?

Mr. Phil Woodward, Pfizer Central Research, United Kingdom

- \* Statistical methods need to be sold to scientists
- \* Regulatory requirements appear to discourage good study design
- \* Standards needed for reporting parameter setting factorial designs

### Optimisation of Process Parameters for Blending and Tableting

Dr. Henrik Melgaard, Novo Nordisk A/S, Denmark

- \* Validation and use of designed experiments in production scale
- \* Prediction of content uniformity from granulation data
- \* Presentation of a case study on blending and tableting

End of the Workshop