Joint DIA/MHRA Statistics Workshop

Event #13107
2-4 October 2013
Hilton London Docklands Riverside Hotel
London, United Kingdom

Programme Committee

Mouna Akacha
Statistical Methodologist, Novartis Pharma AG, Switzerland

Deborah Ashby
Professor of Medical Statistics and Clinical Trials, Co-Director of Imperial Clinical Trials Unit, School of Public Health, Imperial College London, UK

Egbert Biesheuvel
Director Late Development Statistics, Biostatistics and Research Decision Sciences, the Netherlands

Robert Hemmings
Statistics Unit Manager, Licensing Division, MHRA, UK

James Matcham
Director of Biostatistics, Amgen Ltd, UK

John Parkinson
Director, Clinical Practice Research Datalink Division, MHRA UK

Andrew Thomson
Head of Epidemiology, Vigilance Risk Management of Medicines Division, MHRA, UK

Richardus Vonk
Senior Director, Head of Research and Clinical Sciences Statistics, Bayer Pharma AG, Germany

ABOUT DIA

The DIA is a global association of approximately 18,000 members who are involved in the discovery, development, regulation, surveillance or marketing of pharmaceuticals or related products. The DIA is committed to the broad dissemination of information on the development of new medicines or generics, biosimilars, medical devices and combination products with continuously improved professional practice as the goal.

The DIA is an independent non-profit organisation. The voluntary efforts of DIA members and speakers allow the DIA to organise conferences, workshops and training courses and provide publications and educational material.

DIA's headquarters are in Horsham, PA, USA, with the European office in Basel, Switzerland, and other regional offices in Tokyo, Japan, Mumbai, India, and Beijing, China.

For more information, visit www.diahome.org or call DIA Europe on +41 61 225 51 51.

Overview

Life-cycle management is a widely accepted concept for the development and marketing of medicines. At each step of this process, pre- and post-licensing, statisticians work to develop methods that can improve efficiency and can enhance decision-making through optimal study design, analysis and inference. The workshop aims to discuss the latest developments in statistical methodology and decision-making in exploratory development, confirmatory development, licensing decisions and management of benefits and risks post-licensing. The discussions will consider not only the methods themselves, but how best to integrate methods for use in a regulatory context. Beyond this, the meeting seeks to ask whether there are advances in the collection and understanding of real world data that can inform and improve the design of confirmatory clinical trials, and focuses on the practical challenges facing statisticians involved in drug development.

Key Topics

- Latest news on emerging regulatory guidance documents for clinical trial methodology
- Clinical Trial Transparency – practical challenges ahead for statisticians
- Harmonising sponsor and regulator decision-making across the life-cycle, from dose-finding through benefit-risk and beyond; understanding hurdles and optimising methods with a focus on Bayesian Statistics and quantitative benefit risk analysis.
- Therapeutic area special; a focus on biological medicines
- Clinical Practice Research Datalink tutorial
- Incorporating real world data into drug development, licensing, reimbursement and prescribing
- Risk-based monitoring
- Increasing the breadth of sponsor/regulator interactions on methodology

Sessions Will Include

- Clinical Trial Transparency
- Challenges with Biological Medicines
- Emerging Issues in Risk Based Monitoring
- Practical Decision Making across the lifecycle: Bayesian Approaches
- Regulatory Hot Topics

Who Will Attend

Professionals with an interest in the application of and research in statistics in the drug development process from the pharmaceutical industry, academia, regulatory and governmental agencies, as well as contract research organisations.

Continuing Education

DIA meetings and training courses are generally approved by the Commission for Professional Development (CPD) of the Swiss Association of Pharmaceutical Professionals (SwAPP) and the Swiss Society of Pharmaceutical Medicine (SGPM) and will be honoured with credits for pharmaceutical medicine. All participants are eligible for these credits.

PRE-WORKSHOP TUTORIAL ON KEY STATISTICAL TOPICS IN DRUG DEVELOPMENT

Wednesday, 2 October 2013 I 09:00-12:30

Tutorial
DOSE FINDING IN DRUG DEVELOPMENT: CHALLENGES AND SOLUTION

DIA®
www.diahome.org

PRE-WORKSHOP HALF DAY TUTORIAL

08:30 ARRIVAL & TUTORIAL REGISTRATION

09:00 TUTORIAL

10:30 - 11:00 COFFEE BREAK

Tutorial I 09:00 – 12:30

DOSE FINDING IN DRUG DEVELOPMENT: CHALLENGES AND SOLUTIONS

Tutorial Instructor:

Bjoern Bornkamp, Expert Statistical Methodologist – Integrated Information Sciences, Novartis Pharma AG, Switzerland

Byron Jones, Senior Biometrical Fellow/Executive Director – Integrated Information Sciences, Novartis Pharma AG, Switzerland

Historically, the selection of doses for Phase III confirmatory studies has often been poor due to a lack of understanding of the relationship between efficacy and dose. For an informed Phase III dose selection it is essential that the full shape of the dose-response curve is characterised in Phase II trials. Traditional Phase II designs that use a fixed choice of doses and rely on comparisons between doses means can be poor at doing this. Using analysis methods that estimate the complete dose-response relationship and allow the choice of doses to change in an adaptive manner during a Phase II trial lead to more informative studies and ultimately better planning for Phase III.

In this course we will describe methods for dose-response modeling with some focus on the MCPMod methodology, in addition we discuss adaptive dose-finding designs and will describe the main features of the Dose Finding Rpackage. This package implements the methods described in this tutorial and will be illustrated on several examples

Overview

1. Introduction
   - General objectives (design aspects of dose-finding studies)
   - Motivating example (advantages/disadvantages modelling vs ANCOVA
2. Dose-Response Modelling
   - Dose-response models and estimation
   - Introduction to Dose Finding Rpackage
3. MCPMod
   - Introduction
   - Application to example
4. Optimal Designs / Adaptive Design
   - Optimal design theory
   - Adaptive Bayesian dose-finding example

WEDNESDAY | 2 OCTOBER 2013

START OF WORKSHOP

12:30 REGISTRATION AND WELCOME COFFEE

13:30 **Statistics, Evidence and Decision Making**
Karen Facey, Evidence Based Health Policy Consultant, UK

Over the past two decades the role of the statistician in the design, analysis, reporting and regulatory assessment of confirmatory trials has gone from strength to strength. As a wider range decision-makers are now responsible for patient access to new medicines, there is a need for statisticians to influence the entire medicine's development programme. Statisticians need to understand what evidence decision-makers require, how value is interpreted in different contexts and the important role they have to play in bringing rigour and clarity to discussions of risk and uncertainty

14:00 Session 1

CLINICAL TRIAL TRANSPARENCY

Session Co-Chairs:
Egbert Biesheuvel, Director, Late Development Statistics, Biostatistics and Research Decision Sciences, MSD, NL
Rebecca Sudlow, Associate Director Biostatistics Roche Products Limited, UK

There is a significant change coming to Europe regarding access to patient level data. EMA has decided to make individual patients' data from clinical trials available to third parties beginning January 1st, 2014. This session will present the ongoing rapid developments in this area from academic, regulatory and industry perspectives. It will touch upon key topics like ensuring patient confidentiality, data formats and transparency of requests and scientific purpose and will highlight the importance to the EU statistical community.

Presentation title to be confirmed
Christoph Gerlinger, Senior Director, Statistics, Bayer Pharma AG, Germany

Access to Anonymised Patient Level Data from GSK Clinical Trials
Sara Hughes, Head of Clinical Statistics, GlaxoSmithKline, UK

Panel Discussion

15:30 COFFEE BREAK

16:00 Session 1 (continued)

CLINICAL TRIAL TRANSPARENCY

Session Co-Chairs:
Egbert Biesheuvel, Director, Late Development Statistics, Biostatistics and Research Decision Sciences, MSD, NL
Rebecca Sudlow, Associate Director Biostatistics Roche Products Limited, UK

Presentation Title to be Confirmed
Tony Johnson, Senior Scientist MRC Clinical Trial Unit Aviation House

Additional speakers invited

17:30 DRINKS RECEPTION

18:30 END OF DAY ONE

THURSDAY | 3 OCTOBER 2013

09:00 Session 2

CHALLENGES WITH BIOLOGICAL MEDICINES

Session Chair:
James Matcham, Director of Biostatistics, Amgen Ltd., UK

Many biologic at medicines are being developed with the expectation that they may only be effective in a subgroup of patients. Planning a development programme investigating the utility of companion diagnostics and considering the subsequent population enrichment, is an active area of research. This session will provide an opportunity to hear about the current views and activities in the development of companion diagnostics and in population enrichment designs.

Current Thoughts in the Design of Population Enrichment Studies
Andrew Grieve, Senior Vice President Clinical Trial Methodology, Aptiv Solutions, Germany

Can a Treatment be Licensed on the Basis of Post Treatment Predictive Biomarkers?

Andrew Stone, Biometrics & Information Science Head Oncology, AstraZeneca, UK

Case Study

10:30 COFFEE BREAK

11:00 Session 2 (continued)

CHALLENGES WITH BIOLOGICAL MEDICINES

Session Chair:
James Matcham, Director of Biostatistics, Amgen Ltd., UK

Other statistical challenges with Biologic Medicines are in the development of biosimilar versions of original biologic products and in assessing the safety of vaccines. This session provides an opportunity to hear the regulatory review of the first few years of biosimilar product approval and to hear some of the challenges of reviewing the safety of vaccines.

Regulatory Review of The Early Years of Biosimilar Products
David Brown, Expert Statistical Assessor, MHRA, UK

Using Multiple Statistical Approaches to Establish the Safety of Vaccines
Suzie Seabroke, Senior Pharmacoepidemiology Assessor, MHRA, UK

12:30 LUNCH

14:00 Session 3

EMERGING ISSUES IN RISK BASED MONITORING

Session Co-Chairs:

Andrew Thomson, Head of Epidemiology, Vigilance Risk Management of Medicines Division, MHRA, UK
Marc Buyse, Executive Director & Chairman, IDDI & CluePoints, Belgium

Conducting a clinical trial is a risky business. Risk based monitoring is a phrase that can mean different things to different people. The session will focus on two different but important areas. Firstly, how clinical trials can be monitored in a proportional fashion, how risk-based approaches might be adopted, and how new legislation facilitates that. Secondly, how clinical trials can and should be monitored so that risks to the integrity of the trial are picked up, and crucially how statisticians should be involved in the process. The session will conclude with a round table discussion to discuss the issues raised with the wider audience.

Presentation title to be confirmed
Fergus Sweeney, Head of Inspections, European Medicines Agency, UK

Funnels Plots as a Risk Based Monitoring Tool
John Davies, Records Manager, GlaxoSmithKline Inc., UK

Presentation title to be confirmed
Martin Landray, Reader in Epidemiology, Oxford University CTSU, UK

15:30 COFFEE BREAK

16:00 Session 3 (continued)

EMERGING ISSUES IN RISK BASED MONITORING

Session Chair:
Andrew Thomson, Head of Epidemiology, Vigilance Risk Management of Medicines Division, MHRA, UK

Presentation title to be confirmed
Marc Buyse, Executive Director & Chairman, IDDI & CluePoints, Belgium

Challenges with Statistical Validation of Metrics for Risk-Based Monitoring: Reflections on a pilot study
Erika Daly, Manager Biostatistics & Programming, ICON Clinical Research, Ireland

Round Table Discussion

17:30 END OF DAY 2

FRIDAY | 4 OCTOBER 2013

8:30 Session 4

PRACTICAL DECISION MAKING ACROSS THE LIFECYCLE: BAYESIAN APPROACHES

Session Chair:
Richardus Vonk, Senior Director, Head of Research and Clinical Sciences Statistics, Bayer Pharma AG, Germany

As the attrition in late stage clinical development is alarmingly high, much attention is given to the development of clear, quantitative decision criteria throughout clinical development. Bayesian methods are an integral part of the development of such quantitative criteria. The use of Bayesian methodology in clinical development has gained attention in the statistical as well as in the medical area. Focus is on decision making in early clinical trials, but also includes applications to translational medicine and the identification of predictive and prognostic biomarkers. One major challenge is the integration of results obtained from different settings into the design of clinical studies.

The speakers will focus on the application of Bayesian methods to create results that enable decision making in the drug development process.

A Bayesian-based Clinical Utility Index for Dose Determination in Drug Development: Design space thinking applied to clinical development
Bruno Boulanger, CSO, Arlenda S.A., Belgium

The Contribution of Bayesian Methodology to Quantitative Decision Making in Drug Development
Andrew Grieve, Senior Vice President Clinical Trial Methodology, Aptiv Solutions, Germany

Assessing Phase 3 Success Probabilities in Phase 2. A Bayesian Approach
Tony Sabin, Director, Biostatistics, Amgen Ltd, UK

10:00 COFFEE BREAK

10:30 Session 4 (continued)

PRACTICAL DECISION MAKING ACROSS THE LIFECYCLE: QUANTITATIVE BENEFIT RISK ANALYSIS

Session Chair:
John Parkinson, Director, Clinical Practice Research Datalink Division, MHRA UK

Benefit Risk Analysis is increasingly important throughout the lifecycle, from early development, through authorisation where a formal benefit risk balance analysis is performed, and beyond into the wider post-marketing arena, Quantitative methods exist to help facilitate the discussion of how and why the balance is positive (or negative) which leads to the potential for better decisions to be made, and for better communication of decisions. The talks in this session will address the use of statistical and quantitative methods throughout the lifecycle, focussing on real, practical ways such analyses can add value.

Modeling and Simulation in Early Drug Development
Günter Heimann, Global M&S Statistics Head Novartis, Switzerland

Presentation title to be confirmed
Ed Waddingham , NIHR Research Methods Fellow, Imperial College London, UK

Statistical Challenges in Post Licensing Benefit Risk - A Regulatory View
Andrew Thomson, Head of Epidemiology, Vigilance Risk Management of Medicines Division, MHRA, UK

12:00 LUNCH

13:00 Session 5

REGULATORY HOT TOPICS

Session Chair:
Deborah Ashby, Professor of Medical Statistics and Clinical Trials, Co-Director of Imperial Clinical Trials Unit, School of Public Health, Imperial College London, UK

The first part of the regulatory hot topics session will focus on 3 areas where there has been a lot of recent activity, both from regulators and from Industry: subgroup analyses, analysing recurrent event data, and handling missing data. These talks will set the scene for the key challenges in the area, highlighting the challenges for regulators, industry and academia alike.

Hot Topics for Regulators
Rob Hemmings, Statistics Unit Manager, MHRA, UK

Making the Most of Event Outcome Trials: use of recurrent events, not just time to first
Stuart Pocock, Professor of Medical Statistics, London School of Hygiene & Tropical Medicine, UK

The Value of Data obtained after Study Treatment Discontinuation
Mouna Akacha, Expert Statistical Methodologist, Integrated Information Sciences Novartis Pharma AG, Switzerland

14:30 **COFFEE BREAK**

15:00 **Session 5 (continued)**

REGULATORY HOT TOPICS

Session Chair:
Deborah Ashby, Professor of Medical Statistics and Clinical Trials, Co-Director of Imperial Clinical Trials Unit, School of Public Health, Imperial College London, UK

The second half of this session will be a round table discussion, exploring the issues of the previous session but also encompassing the wider issues raised by the whole conference. The panel will include further experts from industry and Regulatory Authorities.

Kevin Carroll, Independent Consultant, UK
David Wright, Expert Statistical Assessor, MHRA, UK

Additional Panel Members

16:00 **END OF WORKSHOP**

HOTEL INFORMATION

DIA has blocked a number of rooms at the:
Hilton London Docklands Riverside Hotel
265 Rotherhithe Street
London SE16 5HW, UK

http://www1.hilton.com/en_US/hi/hotel/LONNDHI-Hilton-London-Docklands-Riverside/index.do

at the special rate of:

£ 139.00 for room and breakfast, exclusive of VAT

Group Name: DIA Europe

To make your reservation please send your booking request to the following email address:

liane.lopes@hilton.com

Or call the reservation team:+44 (0) 207 2311001

Important: Please complete your reservation by 3 September 2013 at the latest. Reservations received after this date will be subject to hotel availability and room rate may vary.

In case of cancellation:

Cancellation of the hotel booking must be made in writing directly to the hotel 45 days prior to the arrival date due to the allocation booking. Cancellations made at least 45 days prior to arrival will not incur any cancellation charges. Any cancellation made less than 45 days prior to arrival will be subject to the first night being charged at the full agreed rate. All no shows will be billed for the entire stay.

DIA EUROPE CONFERENCES AND WORKSHOPS 2013-2014

- **7th Annual Clinical Forum and Exhibition**
  8-9 October 2013 I Dublin, Ireland | ID 13103
- **Combination Products Workshop**
  17 October 2013 I Basel, Switzerland | ID 13106
- **14th Conference on European Electronic Document Management (eDM) and Exhibition**
  20-22 November 2013 I Dublin, Ireland | ID 13110
- **Joint DIA/IMB Common European Submission Platform (CESP) Information Day**
  20 November 2013 I Dublin, Ireland | ID 13111
- **European Healthcare Deciders' Forum**
  January 2014 I Paris, France I ID 13108
- **26th Annual EuroMeeting and Exhibition**
  25-27 March 2014 | Vienna, Austria | ID 14101
- **7th European Conference on Rare Diseases & Orphan Products (ECRD 2014)**
  8-10 May 2014 I Berlin, Germany I ID 14106
- **8th European Forum for Qualified Person for Pharmacovigilance (QPPV)**
  13-15 May 2014 I London, United Kingdom

REGISTRATION FORM

Joint DIA/MHRA Statistics Workshop

2-4 October 2013 I Hilton London Docklands Riverside, London, United Kingdom

DIA www.diahome.org

ID #13107

FEES

	Member	Non-Member
Industry	€ 1'150.00 ❑	€ 1'265.00 ❑
Academia/Charitable/Government/Non-profit (Full-time)	€ 575.00 ❑	€ 690.00 ❑
Join DIA now to qualify for the member rate	€ 115.00 ❑	

PRE-CONFERENCE TUTORIALS (2 OCTOBER 2013)

I wish to attend:

Tutorial 1 - THE USE OF CPRD € 350.00 ❑

Tutorial 2 - DOSE FINDING IN DRUG DEVELOPMENT: CHALLENGES AND SOLUTIONS € 350.00 ❑

TOTAL AMOUNT DUE: _____

If DIA cannot verify your membership upon receipt of registration form, you will be charged the non-member fee.

Group discount/SME rates available. Special rates for students and patient representatives on offer, subject to avaibility – please contact DIA Europe for more information.

Registration fee includes: refreshments, lunches and meeting material.

Payment is due 30 days after registration and must be paid in full by commencement of the event.

ATTENDEE DETAILS

Please complete in block capital letters or attach the attendee's business card here.

❑ Prof ❑ Dr ❑ Ms ❑ Mr

Last Name

First Name

Company

Job Title

Address

Postal Code City

Country

Telephone

Fax

Email*

*(Required for confirmation)

DIA reserves the right to include your name and affiliation on the attendee list.

PAYMENT METHODS

Credit cards: Payments by VISA, Mastercard or AMEX can be made by completing the details below. Please note that other types of credit card cannot be accepted.

❑ **Please charge my** ❑ VISA ❑ MC ❑ AMEX

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❑ **Bank transfers:** When DIA completes your registration, an email will be sent to the address on the registration form with instructions on how to complete the bank transfer. Payments in EURO should be addressed to "Account Holder: DIA." Please include your name, company, Event ID #13107 as well as the invoice number to ensure correct allocation of your payment.

Payments must be net of all charges and bank charges must be borne by the payer. **If you have not received your confirmation within five working days, please contact DIA Europe.**

By signing below, I confirm that I agree with DIA Europe's Terms and Conditions of booking. These are available from the office or on http://www.diahome.org/EUTerms

Date	Signature

Cancellation Policy

All cancellations must be made in writing and be received at the DIA Europe office five working days prior to the event start date. Cancellations are subject to an administrative fee:

- Industry (Member/Non-member) € 200.00
- Academia/Charitable/Government/Non-profit (Full-time) (Member/Non-member) € 100.00
- Tutorial cancellation € 50.00

If you do not cancel five working days prior to the event start date and do not attend, you will be responsible for the full registration fee. DIA Europe reserves the right to alter the venue and dates if necessary. If an event is cancelled or postponed, DIA Europe is not responsible for airfare, hotel or other costs incurred by registered attendees. Registered attendees are responsible for cancelling their own hotel and travel reservations.

Transfer Policy

You may transfer your registration to a colleague prior to the start of the event but membership is not transferable. Substitute attendees will be responsible for the non-member fee, if applicable. Please notify the DIA Europe office of any such substitutions as soon as possible.

Photography Policy

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The DIA Europe Customer Services Team will be pleased to assist you with your registration from Monday to Friday between 08:00 and 17:00 CET.

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