Preliminary Brochure

Inaugural Biological Assays Conference

All 3 days for Under €1000.00

10-12 September 2008, Berlin Germany

Our Expert Presenters:

Gabriele Dallmann
Rose Gaines Das
Stan Deming
Bassam Hallis
Camille Dycke
Alfred Schnüriger
Michael Merges
Cecil Nick
Nadja Prang-Richards
Michael Sadick
Robert Wilson
Karin Havenith
Cornelius Fritsch
Jens Lohrmann
Laurent Fanget
John Dunn
Ralf Stegmann

Key Topics:

- Draft USP Chapter <111> Review
- EP Section 5.3 Perspective
- Regulatory Consequences of Changing the Potency Assay
- Ins and Outs of Potency Calculations
- Parallelism: Global Harmony Undone?
- Regulatory Priorities for Different Bioassays
- Case Studies: ADCC Assay Case Studies and Alternate Assay Strategies
- Case Studies: Transferring Potency Assays
- Case Studies: Vaccine Challenge Potency Assays
- Case Study: Improving speed and accuracy by changing read-outs.

Meeting Organizers:

Laureen Little, Quality Services
C. Jane Robinson, NIBSC
Hans-Joachim Wallny, Novartis Biologics

Not-for-Profit Meeting:

Developed and Run by Scientists for Scientists

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BEBPA's Inaugural Biological Assay Conference

Pre-Conference Workshop on Parallelism

Establishing a formal approach to assessing similarity of the sample vs. reference dose-response curves is a key step in bioassay development. This assessment, simply stated is asking and answering the question, "How parallel is parallel?" Currently both the USP and EP recommend the F-test. However the USP is currently writing a chapter recommending an equivalence testing paradigm. The existence of two distinct approaches in two different pharmacopeias may create problems in the future. This workshop provides background, cases studies and open discussion about this critical topic.

8:30 – 8:40 **Welcome by Workshop Chair**

8:40- 9:00 **Introduction: Parallelism- the problems seen from the bioassayist's viewpoint**

Parallelism of the dose-response curves (or transformed dose-response curves) of biological preparations in a bioassay is one of the fundamental tests for functional similarity of the preparations – but how parallel is parallel? How can we set meaningful limits? What do the pharmacopeia say? What can the bioassayist do?

C. Jane Robinson, Ph.D, Principal Scientist, **NIBSC**

9:00 – 12:00 **Tutorial: It's *Similarity* That's Important: Not Just Geometric "Parallelism"**

The simple, broad concept of *similarity* (often referred to by the narrower, misleading, confusing term "parallelism") has a long history that comes to us through E. C. Wood by way of D. J. Finney. This historical review and tutorial will present the concept of *similarity* and see how it has become distorted and restricted. Understanding the real meaning of "parallelism" allows us to incorporate assessments of all critical parts of the dose response curves when developing biological assays.

Stan Deming, PhD, President, **Statistical Designs**

12:00 – 1:30 Lunch

Case Study Presentations

1:30-2:10 **Case Study #1: Cell-Based Bioassay Development and Fitting the Appropriate Dose-Response Curve**

This presentation summarizes some of the issues that arise during cell-based bioassay development with a focus on the implementation of JMP[ä1] software for fitting the data. Parallel line analysis of cell-based bioassay data consists of plotting the serial dilution curves of an unknown compound and a reference standard. Parallel curves, often nonlinear, result when the unknown compound and reference standard work by the same biological mechanism. [1]JMP[ä] is a trademark of SAS Institute, Inc

Michael Merges, Senior Manager, **Lonza Walkersville**

2:10-2:50 **Case Study #2: Assessing Parallelism Using the PLA 2.x Tool Set**

Ralf Stegmann PhD, CEO, **Stegmann Systems**

2:50-3:30 **Case Study #3: Comparison of Methods Used to Measure Parallelism**

Data from samples with identical material to the reference standards and samples that have been stressed or have impurities will be examined using three methods for assessing parallelism.

John Dunn, PhD, CTO, **Brendan Technologies**

Break: 3:30—4:00

Pharmacoepia Update

4:00—4:40 USP Draft Chapter <111> Review

The USP chapter <111> has been in rewrite for over 5 years. The chapter proposes new approaches, some of which are controversial and contrary to the EP 5.3. This talk will provide a review of the chapter. **Speaker TBA**

4:40—5:20 Review of Recent Revisions to Chapter 5.3 of European Pharmacopoeia

Chapter 5.3 of the EP, covering statistical analysis of results, has recently been updated. The most recent updates are Sub-Sections 7.5: Extended non-linear dose – response curves and 7.6: Non-parallelism of dose – response curves. These changes and their implications will be discussed, with particular reference to the ongoing updating of USP Chapter 111.

Speaker: Rose Gaines Das, PhD CStat

5:30 Workshop Ends

BEBPA: Who are We? What Do We Aim to Accomplish?

The Biopharmaceutical Emerging Best Practices Association (BEBPA) is a not-for-profit association, founded in 2008, managed by and for the benefit of the biopharmaceutical scientific community. BEBPA provides an open international forum for the presentation and discussion of scientific issues and problems encountered in the biopharmaceutical community. .

Three Ways to Register

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BEBPA's Inaugural Biological Assay Conference

Main Conference, Day 1: 11 September, 2008

8:30 Registration, Coffee and Tea

9:00 Chairperson's Opening Remarks
Laureen Little, PhD Principal Consultant **Quality Services**

9:15 Key Note Talk: The right assay format for biotech product development and therapeutic vaccines

The development of highly innovative protein-based therapeutics poses growing challenges for the (bio)analytical development of drug product release assays. This talk covers the choice of the right bioassay format depending on the mode of action, the bioassays' purpose and compliance with the actual regulations.

Nadja Prang-Richard, PhD, MBA, Head of Biotech Product Development, **Merck Serono SA**

Developing Biological Assays

10:15 The Reference and Test Samples Are "Parallel" —Now What?

Bioassays are most often used to estimate an amount of substance or a relative potency. After initially showing that the reference and test samples exhibit "parallel" behavior in the assay (Finney's condition of "similarity"), it remains to calculate the final result and its uncertainty. This talk reviews such statistical calculations for 4PL and slope ratio models.

Stanley N. Deming, Ph.D, President, **Statistical Designs**

11:00-11:30 Break

11:30 Case Study: Satisfying a need for speed (and accuracy and robustness): Conversion of an AlamarBlue-based bioassay to TiterGlo

A common strategy for cell-based bioassays is based upon 'responder' cell proliferation. One of the methods used to quantify the cell proliferation has been the use of the Red-Ox dye AlamarBlue. AlamarBlue assays have been utilized for some time, but have inherent limitations due to their long-term (culture) nature (4 -5 days). The use of a more optimal cell viability quantifying system allows for a more rapid, more accurate and more versatile bioassay. A case study will be presented describing the successful conversion of a 4-day AlamarBlue based bioassay to a more accurate and robust 3-day bioassay based upon TiterGlo luminescence quantification.

Michael Sadick, Ph.D., Senior Scientist/Senior Manager, Biopharmaceutical Analysis, **Aptuit**

12:15-1:30 Lunch

1:30 Chairperson's Opening Remarks
Dr. Hans-Joachim Wallny, Technical Project manager and Bioassay Consultant **Novartis Biologics**

Case Studies for Monoclonal Antibody Products

1:45 Case Study: Assessing Fc receptor interactions of monoclonal antibodies

The pharmaceutical mode of action of many therapeutic antibodies depends on Fc-mediated effector mechanisms. These effector functions are mediated by a family of Fcγ receptors expressed predominantly on certain hematopoietic cell types. We present data on our assays measuring the interaction of monoclonal antibodies with Fc receptors and illustrate the utility of these assays by a case study.

Dr. Cornelius Fritsch Principal Scientist **Novartis Biologics**

2:30 Case Study: Development of a robust CD16a binding ELISA

One of the effects of therapeutic antibodies is the engagement of the immune effector mechanism antibody-dependent cell-mediated cytotoxicity (ADCC). ADCC requires interaction of the therapeutic antibody with target and effector cells. The interaction between therapeutic antibody and Fcγ Receptor on the effector cell is modulated by core fucosylation. Variations in antibody glycosylation can significantly impact antibody activity. We present the development of a robust CD16a binding ELISA that is shown to correlated with glycosylation status and functional activity measured by antibody-dependent cell-mediated cytotoxicity.

Karin Havenith, Ph.D. Principal Scientist **Genmab B.V.**

3:15-3:45 Break

3:45 Case Study: Correlation between ADCC and CD16/ CDR binding assays to assess product functionality

The use of ADDC as a functional bioassay for release testing is impractical. Donor to donor variability and the use of radioactive isotope prohibit its use in a QC setting. We have developed a CD16 binding assay that can be used, in addition to a CDR binding assay, as a surrogate for the ADCC assay. A correlation between these assays and the ADCC assay will be discussed.

Laurent Fanget, M.S, Sr, Manager, **PDL Biopharma Inc**

4:30 Development of an ADCC Assay Suitable for Routine Testing

ADCC activity is an important feature of many therapeutic antibodies. Historically, ADCC assays are known to be laborious, prone to variation and difficult to reproduce. Here we report on the development of an ADCC assay from a purely research-type method to a precise, accurate and reproducible assay.

Alfred Schnüriger, MSc, Group Head Analytical R&D and QC Biotech Products, F. **Hoffmann-La Roche Ltd**.

5:15 End of Conference Day 1

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BEBPA's Inaugural Biological Assay Conference

Main Conference, Day 2: 12 September, 2008

8:00 Registration, Coffee and Tea

8:30 Chairperson's Opening Remarks
Dr. Jane Robinson, Principal Scientist, **NIBSC**

8:45 USP Draft Chapter <111> Comment Period
Come and voice your concerns. This section will be an open discussion. Comments will be included in a formal letter to USP from BEBPA.

Technology Transfer
9:15 Critical rare reagents and equipment during assay transfer

In today's global market place, assay transfers lab-to-lab, across town and around the world are becoming common place. One key to achieving a successful assay transfer is taking care to identify, characterise and track critical reagents and understanding necessary equipment requirements. A case study will be presented highlighting best practices .

Bassam Hallis, PhD, General Project Manager,
Centre for Emergency Preparedness and Response,
Health Protection Agency,

10:00-10:30 Break

10:30 Case Study: Method transfer of a potency assay

Co-development and in-licensing of therapeutic proteins becomes more important in a competitive environment. From an analytical point of view, such projects imply special challenges such as the transfer of potency assays. Potency assays are usually characterized by their high complexity and an inherent assay variability which needs to be addressed during transfer. In a case study, transfer of a binding assay, we will share insights into potential pitfalls and lessons learned. The pro's and con's of co-development vs. method transfer will be discussed.

Dr. Jens Lohrmann Principal Scientist **Novartis Biologics**

Poster Discussion Section
11:15 Short Presentations of Meeting Posters

This session is set aside for 15 minute presentations about submitted posters.

12:00-1:30 Lunch

1:30 Chairperson's Opening Remarks
Laureen Little, PhD Principal Consultant **Quality Services**

Biological Assay for immunogenicity
1:45 Challenge Assays for Vaccine Development

Protection against challenge is the ultimate test of efficacy for anthrax vaccine but requires BL3 containment to conduct the potency test. For logistical and ethical reasons a number of alternatives to anthrax challenge are being investigated. The strategy for development and validation of the challenge potency assay and selection of alternatives will be presented.

Robert Wilson, Sr. Bioassay Scientist **PharmAthene UK, Ltd**

2:30 Analysis of Data from Immunogenicity Assays: Statistical considerations
Immunogenicity assays require statistical consideration from the point of view of assay design and validation, as do all assays. In addition, immunogenicity assays raise the statistical question of how best to describe or characterize the quality and degree of immunogenicity of samples. Various approaches have been suggested, each offers possible advantages but suffers from some limitations. Topics are:

- Inter assay and inter laboratory comparisons
- Use of control samples in design and analysis
- Role of reference preparations (antigen, antibody)

Rose Gaines Das, PhD CStat

2:30-3:00 Break

Regulatory Considerations
3:00 Regulatory implications of assay outsourcing

Potency assays are increasingly complex and require specialisation. Other assays such as those used to investigate PD or PK parameters in non-clinical and clinical samples are often required for a limited time period only. Thus, they are increasingly performed by external laboratories. The talk provides criteria which should be followed by sponsors and contract laboratories to get assays adequately established, validated and conducted either for short-term or long-term agreements.

Dr. Gabriele Dallmann Director Biopharmaceuticals **NDA Advisory Board**

3:45 The Value of Biossays in Comparability and Biosimilarity Programs
Changes in process can impact the higher order structure of proteins which can impact both efficacy and safety, notably immunogenicity. Since physico-chemical testing is generally not accepted as sufficiently sensitive to detect every subtle but critical change to a protein, the bioassay can play a critical role. This talk coverz:

- The benefits of having more than one bioassay
- Value of in vivo, cell based and biochemical assays
- How predictive is the bioassay
- Can the bioassay replace clinical efficacy data

Cecil Nick Vice President **PAREXEL Consulting**

4:30 Key area of investigation to troubleshoot biological assays

Within the biotech department of Covance laboratories, in Harrogate, UK, the biopotency group focuses on transferring biopotency assays from biopharmaceutical and biotech companies. Whether it is during the development of bioassays or for transfer of validated methods, troubleshooting is always challenging and could have a significant impact on timelines, due to the variety of potential causes that need to be investigated.

Camille Dycke, PhD Manager Biopotency **Covance**

5:15 Conference Adjourns

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