

Second Annual

PEGS EUROPE

5-7 October 2010

Protein & Antibody Engineering Summit

Exhibition Grounds | Hannover | Germany

5-6 October

- **Novel Antibody Constructs and Alternative Scaffolds**
- **Protein Expression and Cell Line Development**

6-7 October

- **Empowered Bispecific Antibodies**
- **Difficult Protein Expression and Purification**

KEYNOTE PRESENTERS:



Josefin-Beate Holz
Chief Medical Officer
Ablynx NV



Bernhardt L. Trout
Ph.D., Director, Novartis-MIT Center
for Continuous Manufacturing



John Birch
Ph.D., CSO, Biopharmaceuticals,
Lonza Group



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PRE-CONFERENCE SHORT COURSE*

Monday, 4 October

14:00 – 17:00

Protein Aggregation in Biopharmaceutical Products

This workshop will discuss the capacity of protein aggregates to increase immunogenicity and will feature case studies and interactive discussions on mechanisms of aggregation, detection and quantitation of aggregates, characterization tools, visible and sub-visible protein aggregation detection and analysis techniques, prevention of particles, impact of aggregation on production, and aggregates as an inducing factor for immunogenicity.

- Mechanistic Perspectives on Aggregation
- Tools and Methods for Analysis
- Approaches for Managing or Preventing Aggregation Issues

Course Instructors:

Tudor Arvinte, Ph.D., Co-Founder, Therapeomic Inc.; Professor, Department of Pharmaceutics, University of Geneva

Martinus Capelle, Ph.D., Scientist and Project Manager, Therapeomic Inc.

Sylvia Kiese, Ph.D., Formulation Scientist, Formulation R&D Biologics, Formulation Research, pRED, Hoffmann-La Roche Ltd.

Agenda:

13:30 – 14:00 Afternoon Short Course Registration

14:00 – 14:15 Chairperson's Introduction

14:15 – 14:35 Complexity and Diversity of Protein Aggregation Mechanisms

Tudor Arvinte, Ph.D., Co-Founder, Therapeomic Inc.; Professor, Department of Pharmaceutics, University of Geneva

The talk will present protein case studies and newly developed analytical methods to analyze protein aggregation in formulations in conditions as near as possible to those in which the drug is applied in vivo. By such complementary methods it is possible to better understand the mechanisms of protein aggregation under a broad range of aqueous conditions.

14:35 – 14:55 The Characterization of Protein Aggregation using Light Scattering Techniques

Bernd Tartsch, Ph.D., Application Specialist Proteins, GPC/SEC and light scattering techniques, Malvern Instruments GmbH

Aggregation is a common issue encountered in the isolation of proteins and during the manufacture of biotherapeutics. The characterization of the aggregation process is hence key and much work has gone in to developing methods for detection and characterisation of aggregates. Chromatographic and light scattering techniques are often used as stand-alone techniques. In the lecture it will be shown that by combining the two, protein aggregates can be readily characterized by determination of their molecular weight and hydrodynamic radius. This is possible in a single measurement with a small amount of sample. It will also be explained how the techniques can help to optimise the PEGulation process and the characterization of protein conjugates.

14:55 – 15:15 High-Throughput Methods to Investigate Protein Aggregation

Martinus Capelle, Ph.D., Scientist and Project Manager, Therapeomic Inc.; Basel

High-throughput (HT) methods are increasingly used not only for drug discovery but also for the characterization of protein properties. The talk will present novel analytical high throughput technologies to probe protein aggregation and conformation changes. As a case study, the

stability of salmon calcitonin will be presented. Approaches to formulate proteins using HT methods will be discussed.

15:15 – 15:45 Refreshment Break

15:45 – 16:05 Aggregation, a Common Challenge during Protein Formulation Development

Sylvia Kiese, Ph.D., Formulation Scientist, Formulation R&D Biologics, Formulation Research, pRED, Hoffmann-La Roche Ltd.

This presentation will offer an industry perspective on one of the major challenges in biologics formulation development. How those challenges were overcome will be shared in various case study examples.

16:05 – 17:00 INTERACTIVE PANEL DISCUSSION:

What are Your Challenges and How Can You Learn from Others – Interactive Q&A with Speakers and Attendees

- Understanding Protein Aggregation Mechanisms
- Pros and Cons of Tools and Methods for Analysis
- Approaches for Managing or Preventing Aggregation Issues

17:00 Close of Protein Aggregation in Biopharmaceutical Products Short Course

About the Workshop Leaders:

Tudor Arvinte was born in Romania in 1956, received his Ph.D. in biophysics from the University of Düsseldorf, Germany. He held research positions in Europe (Max-Planck-Institute, C.N.R.S.) and in U.S.A. (Cornell University and Texas A&M University). He joined Ciba-Geigy in England, and then Ciba-Geigy and Novartis in Basel where he was Head of Exploratory Formulation for biotech products. T. Arvinte worked on the formulation of more than 80 proteins and peptides, has 70 publications and 12 patents. He is Invited Professor at the School of Pharmacy, University of Geneva. In 2003 T. Arvinte co-founded Therapeomic, Inc., a biotech company focused on developing formulations for biopharmaceuticals in collaborations with pharmaceutical companies.

Martinus Capelle obtained his pharmacist diploma in 2001 from Utrecht University in the Netherlands. He obtained his PhD at the University of Geneva - Switzerland, entitled: "High Throughput Formulation of Biopharmaceuticals." Since 2007, he is working as a scientist and project manager at Therapeomic Inc. implementing high throughput analytical methods for characterization, formulation and development of biopharmaceuticals.

Sylvia Kiese holds a B.Sc. (Hons.) degree in Biochemistry and a B.Sc. degree in Biochemistry and Microbiology, both obtained from Rhodes University, Grahamstown, South Africa. She later obtained her Ph.D. from Ludwig-Maximilians-Universität, Munich, Germany in collaboration with F. Hoffmann-La Roche, Basel Switzerland. Sylvia has worked in the area of Formulation R&D Biologics since 2002 initially at Pfizer (UK) and subsequently at Roche (Basel, Switzerland) where she currently holds a position of a Formulation Scientist and Galenical Project Manager.

Bernd Tartsch finished his studies of chemistry and physics at university of Ulm in 1999. After that he worked in a combined project form Institute of Macromolecular Chemistry University Ulm and RWTH Aachen for his the PhD thesis and obtained his PhD in 2003. Subsequently in his role as Technical Sales Specialist at Viscotek GmbH, he was involved in GPC/ SEC projects developing customer solution for polymers, biopolymers and proteins. 2008, following the Viscotek acquisition form Malvern he became Application Specialist Proteins at Malvern Instruments GmbH, which position he currently holds.

*Separate Registration Required.

Sponsoring Organizations



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Novel Antibody Constructs and Alternative Scaffolds

5-6 October

TUESDAY, 5 OCTOBER

9:00 Conference Registration and Morning Coffee

Engineering the Fc Regions for Antigen Binding, Effector Function and Enhanced Half-Life

9:30 Chairperson's Opening Remarks

Christian Heinis, Ph.D., Laboratory of Therapeutic Proteins and Peptides, Institute of Chemical Sciences and Engineering, Ecole Polytechnique Fédérale de Lausanne (EPFL)

9:35 Modular Antibodies: Introducing Antigen-Binding Sites in the Fc Region of IgG

Max Woisetschläger, Ph.D., Director, Target Biology, f-star

We have developed two novel antibody formats: Fcabs, in which antigen-binding sites are introduced into a human Fc fragment; and mAb2s, in which additional binding sites are engineered into the Fc of an intact antibody. Fcabs allow small therapeutic antibody fragments to be isolated that retain all normal antibody functionalities (antigen binding, effector functions and long half life) while mAb2s represents an elegant way to create bispecific antibodies. Examples will be described demonstrating the potential of these proteins as next generation therapeutic biologicals.

10:05 IL-17 Neutralizing Fynomers: Making Use of Fc Fusion Proteins

Dragan Grabulovski, Ph.D., Chief Scientific Officer, Covagen, A.G.

We describe the design, construction, characterization, and use of a large human Fyn SH3 library comprising 8.5×10^{10} individual clones (termed Fynomers). The versatility and broad applicability of the Fynomer technology will be presented as well as the *in vitro* and *in vivo* characterization of high-affinity Fynomers binding to IL-17. We will demonstrate how engineered Fynomer-Fc fusion proteins having appropriate physico-chemical and *in vivo* half-life properties are attractive drug candidates for pre-clinical and clinical development.

10:35 Coffee Break

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Novel Delivery Products

11:00 Exploiting the Biophysical Properties of Centyrins for Alternative Routes of Delivery

Steve Jacobs, Ph.D. Principal Scientist, Centyrex Venture, Johnson & Johnson, Inc.

Alternative scaffolds represent an emerging class of protein drugs that combine the attractive specificity properties of mAbs with the simplicity, ease of manufacture and tissue penetration associated with small molecules. We are exploiting the properties of an exceptionally stable alternative scaffold to develop a series of molecules tailored for alternative routes of delivery. The development and application of the Centyrin technology will be presented, together with *in vitro* and *in vivo* characterization of high-affinity Centyrins against an array of therapeutic targets.

11:30 Anticalins: A Differentiated Biologics Drug Class for Novel Delivery, Broad Target Space and New Modes of Action

Kristian H. Jensen, Ph.D., Chief Operating Officer, Pieris AG
Anticalins are modified versions of human lipocalins. Pieris' lead project PRS-050 (VEGF antagonist) is now entering human studies. Unique features of this drug class such as the ability to bind therapeutically relevant hapten targets will be presented with their broad formulation and delivery options and formatting flexibility.

12:00 Glycan-Binding Decoy Proteins with Strong Anti-Inflammatory Activity Derived from the CellJammer® Platform Technology

Andreas Kungl, CSO, ProtAffin Biotechnologie AG

ProtAffin is developing novel biopharmaceuticals targeting protein-glycan interactions in inflammation. The importance of especially glycosaminoglycans in regulating protein function has been under-exploited as a basis of therapeutics for a long time mainly due to the complexity of this glycan class which prevents easy chemical synthesis. ProtAffin's CellJammer® discovery platform takes advantage of a protein's natural glycan-binding function to improve it thereby generating unique decoy proteins with anti-inflammatory, anti-metastatic or anti-angiogenic activity.

12:30 Lunch for Purchase in the Exhibit Hall

13:45 Dedicated Poster Viewing in the Exhibit Hall

Technologies that Select for Enhanced Half-Life and Stability

14:30 Chairperson's Remarks

Josefin-Beate Holz, Chief Medical Officer, Ablynx NV

14:35 From Clinical Imaging to Serum Half-Life Extension Using HER2-Specific Affibody Molecules

Fredrik Y. Frejd, Ph.D., Project Manager, Biotherapeutics, Affibody AB

Affibody molecules are 6.5-7 kDa scaffold proteins with rapid *in vivo* kinetics. Pre-clinical data leading to clinical trial regulatory approval for a HER2-targeting Affibody imaging agent will be presented. The half life and distribution profile of the imaging molecule was enhanced using albumin binding technology, allowing for successful targeted radionuclide therapy in xenografted mice. Furthermore, the albumin binding technology is general, as shown in a pharmacodynamic study in rats using modified G-CSF associating with albumin.

15:05 PASylation: A Superior Technology to Extend the Plasma Half-Life of Therapeutic Proteins

Arne Skerra, Ph.D., CEO, XL-protein GmbH

PAS sequences form conformationally disordered biological polymers with large hydrodynamic volume and high solubility, similar to PEG. In contrast, PASylated biopharmaceuticals can be directly produced in microbial expression systems with a wide range of therapeutic proteins, thus avoiding costly and laborious chemical modification steps. PAS sequences can prolong the pharmacokinetics of biologics in mice by a factor of 10-100. Preclinical data for several pharmaceutically attractive protein drug classes, including antibody fragments and alternative scaffolds, will be presented.

15:35 Refreshment Break

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Focus on Screening and Selection of Drug Candidates for Specific Purposes

16:00 Sponsored Presentation (Opportunity Available)

16:30 Tn3: A New Platform for Non-Antibody Protein Drugs

Manuel Baca, Ph.D., Principle Scientist, Antibody Discovery & Protein Engineering, MedImmune, Inc.

17:00 Generating A Best-in-Class DARPIn Therapeutic for the Treatment of Ophthalmic Neovascularization Diseases

H. Kaspar Binz, Ph.D., Vice President Technology, Molecular Partners AG
DARPins combine the advantages of antibodies with those of



small molecule drugs and allow us to generate a broad pipeline of innovative new drug candidates in a short time. We will present hands-on data on how we choose the best of the many drug candidates and how we assay them *in vitro* and *in vivo*. This process will be illustrated by the example of a best-in-class therapeutic DARPin for the treatment of wet AMD and other ocular neovascularization diseases.

17:30 Challenges in Domain Antibody Development

Thomas Sandal, Head, Microbial Process Research, GlaxoSmithKline Research & Development

GSK has developed an innovative approach for assessing the development of potential novel domain antibodies (dAbs). The strategy comprises high-throughput and downscaled methods to evaluate the biophysical properties and purification challenges for a range of dAbs. In order to develop a commercially viable expression system, a high-throughput method has been implemented to screen a combination of recombinant vector designs and host strains. This high-throughput screening technique facilitates the selection of a production strain and vector based on the productivity and quality of dAb.

18:15 Interactive Breakout Discussion Groups

19:15 – 21:00 CHI Networking Reception *Sponsored by*



WEDNESDAY, 6 OCTOBER

9:00 Conference Registration and Morning Coffee

Accessing Difficult to Reach Targets

9:30 Chairperson's Opening Remarks

Thomas Sandal, Head, Microbial Process Research, GlaxoSmithKline Research & Development

9:35 KEYNOTE PRESENTATION



Exploiting Nanobody® Advantages to Target Challenging Proteins: From Discovery to *in vivo* Proof-of-Concept for an Anti-GPCR Nanobody

Josefin-Beate Holz, Chief Medical Officer, Ablynx NV

Nanobodies are therapeutic proteins based on the smallest functional fragments of heavy chain-only antibodies. These stable, naturally evolved single-domain binding structures can target less accessible epitopes and can be formatted into highly potent drug candidates for challenging target classes including GPCRs and ion channels. Using the anti-CXCR4 Nanobody, ALX-0651, as a case study, data from initial discovery through to pre-clinical *in vivo* animal model validation will be presented to highlight inherent properties of Nanobodies that makes them well-suited for drug development.

10:05 scFv Antibody Fragments for Ocular Therapies

David Urech, Ph.D., Head, Research & Development, ESBAtech LLC, an ALCON Biomedical Research Unit

Due to their low molecular weight (26 kDa) and the resulting pharmacokinetic properties, single-chain antibody fragments qualify for local therapies and delivery routes that have not yet been explored for full-size antibodies and larger fragments thereof. Stable naturally occurring variable domain scaffolds allow engineering scFvs with drug-like properties. ESBA105 is a humanized anti-TNF scFv, developed for the treatment of inflammatory ocular diseases as well as for osteoarthritis. This antibody fragment, upon administration to the ocular surface by eye drops, penetrates into all ocular compartments and reaches therapeutic concentrations in the aqueous and the retina. Preclinical efficacy with topical application of eye drops containing ESBA105 is shown in the monkey laser-injury model for choroid neovascularisation.

10:35 Coffee Break

Sponsored by



Focus on Affinity and Specificity

11:00 XTENylation Enables Long Half-Life and Maximum *in vivo* Potency via Precise Tuning of Drug-Target Affinity

Volker Schellenberger, Vice President, Drug Discovery, Amunix, Inc.

The design of biopharmaceuticals with long *in vivo* half-life requires slowing all drug clearance mechanisms. Amunix has developed protein sequences with PEG-like properties that can be directly fused to a protein drug to increase the hydrodynamic radius and prevent kidney elimination. Careful optimization of XTEN size and fusion site allows the precise tuning of drug-target affinity in order to reduce receptor-mediated clearance while retaining high *in vivo* potency.

11:30 Bicyclic Peptides with Tailored Binding Specificities

Christian Heinis, Ph.D., Laboratory of Therapeutic Proteins and Peptides, Institute of Chemical Sciences and Engineering, Ecole Polytechnique Fédérale de Lausanne (EPFL)

We are generating bicyclic peptide ligands with high affinities and specificities for disease targets using an approach that I have recently developed with Sir Greg Winter at the Laboratory of Molecular Biology (LMB) in Cambridge, UK. Briefly, phage-encoded linear peptides are chemically modified to obtain combinatorial libraries of bicyclic peptides and subjected to affinity selections. The bicyclic peptides combine key qualities of antibody therapeutics (high affinity and specificity) and advantages of small molecule drugs.

12:00 ISMIP™ and SCORPION™ Proteins: Novel, Mono- or Multi-Specific Therapeutic Proteins for Oncology and Autoimmune Diseases

Kendall M. Mohler, Ph.D., Senior Vice President and Chief Scientific Officer, R&D, Trubion Pharmaceuticals, Inc.

SMIP proteins are single-chain, mono-specific molecules which have demonstrated clinical activity in both oncologic and autoimmune diseases. SMIP proteins are smaller than conventional mAbs and can demonstrate distinct signalling properties. Clinical data in patients treated with SMIP proteins will be reviewed. In addition, multi-specific molecules (SCORPION proteins) have been developed. SCORPION molecules which neutralize two soluble targets or deliver tolerogenic cytokines (e.g., IL-10) to antigen-presenting cells have been developed. In comparison to mono-specific proteins, the SCORPION molecules have demonstrated enhanced activity both *in vitro* and *in vivo*.

12:30 Lunch for Purchase in the Exhibit Hall

13:00 Dedicated Poster Viewing in the Exhibit Hall

13:30 Close of Conference



Protein Expression and Cell Line Development

5-6 October

TUESDAY, 5 OCTOBER

9:00 Conference Registration and Morning Coffee

Vectors, Tags, Chaperones, and Genes

9:30 Chairperson's Opening Remarks

9:35 KEYNOTE PRESENTATION



Protein Expression in Mammalian Cells: Past Perspective, Future Potential

John Birch, Ph.D., Chief Scientific Officer, Lonza

More than half of all licensed recombinant therapeutic proteins are produced in mammalian cell systems. The development of efficient expression technologies, in combination with improved feeding strategies in fed-batch culture, has resulted in titres of grams per litre for well-expressed proteins such as antibodies. This talk will cover the key developments that led to this success and the challenges and opportunities that remain.

10:05 A Novel Fusion System for Soluble Overexpression of Recombinant Proteins in *Escherichia coli*

Sofia Costa, Researcher, Biological Engineering, IBCEB, University of Minho

A gene fusion technology has been applied in the *E. coli* system. A novel and promising fusion system, consisting of two fusion tags – Fh8 and H tags, has recently been discovered and patented. Both fusion tags increased protein production yields in *E. coli* and may potentially promote a solubilization effect on difficult-to-express proteins with diagnostic/therapeutic application.

10:35 Coffee Break

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11:00 Production of Recombinant Human Multi-Protein Transcription Factor Complexes

Arnaud Poterszman, Ph.D., Research Director (CNRS), Structural Biology and Genomics, IGBMC-CERMB

We present strategies for production of multi-subunit transcription factors such as nuclear hormone receptor complexes or the basal transcription/DNA repair factor TFIID using the baculovirus expression system. Selected examples illustrate recent developments: (i) HTP mini expression screening, (ii) fluorescent proteins as markers and for quality control (iii) vector development for parallel cloning and (co-) expression of multiple constructs for a single target, (iv) single virus co-expression of multi-subunit complexes.

11:30 Minicircles (MCs): Overcoming the Limitations of Transient Expression Systems

Juergen Bode, Ph.D., Professor, Medical School Hannover

We discuss a ~4kb minicircle (MC), with superior nuclear transfer and expression characteristics due to its ccc-status. Following the initial expression phase MCs are able to exploit the cellular machinery to replicate in a way reminding of ARS-vectors. Several MCs can be established side-by-side allowing the regulated expression of multi-subunit proteins. Genetic elements remaining in the minicircle (promoter, S/MAR, poly(A)-site) and the MC preparation procedure could continuously be refined.

12:00 How a Strong Expertise in Target Proteins Expression can Become an Added Value for Bioprocess Development

Hervé Ginisty, Ph.D., CSO, GTP Technology

In the field of recombinant protein expression, experience and know-

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how are often the key to success. During the past ten years, GTP has worked on more than 800 projects concerning the expression of over 400 challenging proteins. In this presentation, we will outline how the large range of expression systems and purification strategies we have developed, allowed us to address most target proteins expression challenges, and now enable us to offer original and flexible solutions for bioprocess development projects.

12:15 From EnBase to EnPresso - Novel Instant Solutions Facilitate High Level Recombinant Protein and Plasmid Production

Peter Neubauer, Ph.D., Professor, Technische Universität Berlin, and Scientific Advisor, BioSilta Oy

Recently BioSilta have developed a new high cell density culture portfolio, EnBase®, which is based on a biocatalytically controlled release of glucose from glucose polymers. EnBase® can be applied in shaken cultures without any external feeding devices over a wide range of culture volumes and has proven its strength in many laboratories. New research focused on a further simplification of the practical usability of EnBase®, resulted in the development of the EnPresso™ product line, which contains tableted or granulated sterile packed microbial cultivation media which can simply be added to pre-sterilized water. This product line paves the way for direct process scaling from microlitre to pilot-scale cultivations.

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12:30 Lunch for Purchase in the Exhibit Hall

13:45 Dedicated Poster Viewing in the Exhibit Hall

Novel Hosts and Unique Platforms

14:30 Chairperson's Remarks

14:35 A High-Throughput Microtiter Plate-Based Screening Method for the Detection of Full-Length Recombinant Proteins

Matthias Mack, Ph.D., Head, Institute for Technical Microbiology, Mannheim University of Applied Sciences

Escherichia coli is an important host for the production of proteins. The development/optimization of a protocol to overproduce a desired protein in *E. coli* is often tedious. A novel high-throughput screening method based on the Luminex® xMAP™ bead technology was developed allowing a rapid evaluation of a certain expression strategy. The new method was also applied to the analysis of proteins produced in *Pichia pastoris* and *Pichia angusta*.

15:05 Robo-Lector – A Novel Platform for Automated High-Throughput Cultivations in Microtiter Plates with High Information Content

Frank Kensy, Managing Director, m2p-labs GmbH

The presentation will introduce the novel RoboLector platform for automated microbial and cell culture cultivations. 48 or 96 parallel fermentations in a microplate format can be operated and manipulated by a liquid-handling robot triggered by non-invasive online monitoring signals such as biomass and fluorescent protein concentrations, pH and pO₂. Data from a 2-D induction profiling of *E. coli* cultures expressing a FMN-binding fluorescent protein (FbFP) and several examples of media optimization will be presented.

15:35 Refreshment Break

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16:00 Boosting Secreted Expression of Biologics from *Pichia Pastoris* with Novel Tools and Technologies

Thomas Purkarthofer, Ph.D., Head of Business Development, VTU Technology GmbH

Pichia pastoris represents an intriguing expression system for biologics production featuring notable expression and secretion power and cost and safety advantages. VTU applies its exclusive library of synthetic AOX1 promoter variants which trigger a substantial increase in productivity. A well characterized in-house expression toolset and specialized handling protocols ensure to shrink development timelines and ramp up speed-to-clinic. The company's most recent development comprises novel AOX1 variants functioning without induction by hazardous methanol outperforming the (methanol-free) constitutive GAP promoter. Showcase examples applying this powerful *Pichia* system both in the presence and in the absence of methanol will be presented.

16:30 A Novel T7 RNA Polymerase-Dependent Expression System for High-Level Protein Production in the Phototrophic Bacterium *Rhodobacter capsulatus*

Thomas Drepper, Ph.D., Institute of Molecular Enzyme Technology (IMET), Heinrich-Heine-Universität Düsseldorf

17:00 Rapid Protein Quantification by Applying BioLayer Interferometry

Arnout Gerritsen, Director Assay & Bioanalytical Science, Genmab

17:30 *Lactococcus lactis* P170 Expression System: A Novel Secretion-Based Expression System for Production of Recombinant Proteins

Soeren Madsen, Ph.D., Group Leader, Bacterial Expression, Bioneer A/S
The P170 Expression system is based on the endotoxin-free Gram positive bacterium *Lactococcus lactis*. Gene expression is auto-induced during the transition to the stationary phase and the expression system is designed to secrete the recombinant proteins to the growth medium thereby making downstream processing more convenient. Examples will be given on production of recombinant proteins, which has entered phase II clinical trials.

18:15 Interactive Breakout Discussion Groups

19:15 – 21:00 CHI Networking Reception



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10:35 Coffee Break

Advances in Protein Science

11:00 CAP: A New Protein Production Platform based on Immortalized Human Amniocytes

Hartmut Tintrup, Ph.D., Director Marketing & Business Development, Cevac Pharmaceuticals GmbH

Human CAP (CEVEC's Amniocyte Production) cells allow for stable and high yield production of recombinant proteins, with excellent biologic activity and therapeutic efficacy, as a result of authentic posttranslational modification. Based on CAP cells a transient expression system has been developed, that enables extremely high production yields of recombinant proteins within a few days. Thus, CAP and CAP-T technologies offer the use of only one unique platform for early preclinical development through to clinical supply of recombinant biotherapeutics.

11:30 *Pseudomonas* for Protein Expression: Learning from Versatile Hosts

Frank Rosenau, Ph.D., Head, Microbial Expression Technology Group, Institute of Molecular Enzyme Technology, Heinrich-Heine-University Duesseldorf

Their extreme physiological and metabolic versatility qualifies bacteria of the genus *Pseudomonas* as robust and promising strains for biotechnological applications. They are used as expression strains for the production of proteins and secondary metabolites. A system for co-expression of all *Pseudomonas* chaperones allows their transfer and use of the enormous protein folding capacity in other expression strains.

12:00 Protein Aggregation Profile of the Bacterial Cytosol

Salvador Ventura, Ph.D., Group Leader, Institut de Biotechnologia Biomedicina, Universitat Autònoma de Barcelona

The aggregation behaviour of a given polypeptide is strongly influenced by the intrinsic properties encoded in its sequence. We have developed a computational approach to approximate the aggregation profile of an experimental cytosolic *Escherichia coli* proteome. The analysis indicates that the aggregation propensity of bacterial proteins is associated with their length, conformation, location, function and abundance. Overall, the study suggests that the avoidance of protein aggregation in functional environments acts as a strong evolutionary constraint on polypeptide sequences.

12:30 Lunch for Purchase in the Exhibit Hall

13:00 Dedicated Poster Viewing in the Exhibit Hall

13:30 Close of Conference

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WEDNESDAY, 6 OCTOBER

9:00 Conference Registration and Morning Coffee

Mammalian Cell Expression

9:30 Chairperson's Opening Remarks

9:35 Transient Expression in CHO cells: A Balancing Act between Multiple Parameters

Bernd Voedisch, Ph.D., Postdoctoral Researcher, Geisse Group, Novartis
Transient recombinant protein production in CHO cells is gaining steadily momentum in order to better align activities in R&D and to provide a different host cell background potentially impacting the biological performance of the target molecule. Yet, CHO cells are much less amenable to efficient transient expression than HEK293 cells, necessitating an optimal interplay of cell line, expression vector, culture medium and process which is the focus of this talk.

10:05 A Pipeline for the Production of Glycoproteins for Structural Biology

Raymond Owens, Ph.D., Oxford Protein Production Facility, Wellcome Trust Centre for Human Genetics

Obtaining structural information from glycoproteins presents significant technical challenges due to the effects of glycosylation on crystallization. We have developed methods to address these issues and have assembled a semi-automated pipeline for producing and crystallizing glycoproteins. The application of the pipeline to solving the structure of a number of glycoprotein complexes will be presented.



Inaugural

Empowered Bispecific Antibodies and Antibody-Drug Conjugates

6-7 October

WEDNESDAY, 6 OCTOBER

13:00 Conference Registration

Improving Targeting with Antibody-Drug Conjugates: Addressing Selectivity and Delivery

14:00 Chairperson's Remarks

Stefan Barth, Ph.D., Head, Department of Pharmaceutical Product Development, Fraunhofer IME

14:05 Recombinant Human Multi-Domain Fusion Proteins

Stefan Barth, Ph.D., Head, Department of Pharmaceutical Product Development, Fraunhofer IME

Activated and dysregulated macrophages play a decisive role in the development of numerous inflammatory processes including progression of cancer. We have generated novel recombinant multi-domain immunotherapeutics by fusing different cytotoxic enzymes to a single chain fragment derived from the CD64-specific human antibody H22. Final aim is the application of tailor-made immunofusions not only considering the targeting moiety, but also the appropriate cytotoxic agent to specifically destroy diseased cells.

14:35 Antibodies-Conjugated Nanoparticles for Targeted Drug Delivery

Roland Kontermann, Ph.D., Professor, Biomedical Engineering, Institute of Cell Biology & Immunology, University of Stuttgart
Nanoparticles such as liposomes and polymers are versatile carrier systems for delivery of therapeutic molecules, e.g. chemotherapeutic drugs, siRNA and proteins. Conjugation of antibodies, antibody fragments or antibody-mimetic scaffolds to the particle surface allow for active delivery to target cells, e.g. for tumor therapy. Binding to target cells has been shown to promote intracellular uptake and can improve selectivity and therapeutic efficacy. Examples for the generation and application of various targeted nanoparticulate drug carriers will be presented.

15:05 Toxicity-Reducing Potential of Extracorporeal Affinity Adsorption Treatment in Combination with Empowered Antibodies in a Syngeneic Rat Tumor Model

Rune Nilsson, Ph.D., Associate Professor, Department of Oncology, Lund University

Extracorporeal affinity adsorption (ECAT) is a method that safely and efficiently reduces dose limiting toxicity associated with the administration of monoclonal antibodies conjugated with a cytotoxic payload. We have shown that in combination with ECAT higher doses of both radiolabeled (90Y and 177Lu) and drug-conjugated (auristatin) antibodies can be increased without increase of toxicity. During ECAT the circulating antibodies remaining in the blood is removed by in-line passage of the blood through an affinity adsorbent.

15:35 Coffee Break

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16:00 Selected Poster Presentations

18:30 – 21:00 BIOTECHNICA Night: Beer Hall, Full Dinner Reception, Live Band

(Please register to reserve your complimentary ticket ahead of time. No tickets will be available on-site.)

THURSDAY, 7 OCTOBER

9:00 Conference Registration and Morning Coffee

New Bispecific and Multi-Valent Constructs: Optimizing Discovery for Best Results Downstream

9:30 Chairperson's Remarks

Lutz Jermutus, Ph.D., FRSC, Senior Director, Technology, MedImmune

9:35 Optimization of Variable Domain Combination, Orientation and Linkers to Construct Dual Variable Domain (DVD) – IgTM Molecules

Tariq Ghayur, Ph.D., Senior Principal Scientist & Research Fellow, Biologics, Abbott Bioresearch Center, Inc.

Bispecific antibodies (bsAb) offer great therapeutic potential. However, many of the bsAb formats reported require optimization of various drug-like properties to be therapeutically viable. We have recently reported on a novel format termed dual variable domain (DVD) – IgTM. Various approaches used to optimize mammalian cell expression, function and physical stability of DVD-IgTM molecules will be discussed.

10:05 Novel Multispecific Construct

Peter Kiener, CEO, Zyngenia

Multispecific antibody-based therapeutic drugs will be discussed that retain the structural and functional properties of traditional mAbs. These engineered proteins incorporate additional target-binding domains through the fusion of polypeptides, called Molecular Recognition Domains (MRDs), to the Ig heavy and light chains. The antibody has two copies of each MRD and each MRD independently binds its respective target(s) thereby achieving bivalent binding across multiple specificities. MRDs can be designed to enhance binding of the core mAb to cells, tissues and soluble factors.

10:35 Coffee Break

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11:00 Development of a Bispecific TandAb for Clinical Studies: Issues Relating to Immunogenicity, Production and Formulation

Melvyn Little, Ph.D., CSO, Affimed Therapeutics AG

TandAbs are tetravalent bispecific dimeric molecules constructed solely of antibody variable domains. They comprise two binding sites for binding a tumor cell and two further binding sites for binding an immune killer cell. This talk will focus on the challenges faced in developing a bispecific TandAb for the treatment of Hodgkin's lymphoma.

11:30 Bispecific T Cell-Engaging Antibodies of the BiTE Class

Markus Muenz, Ph.D., Associate Director, EpCAM Research, Micromet

The presentation will demonstrate that BiTE antibodies can be generated to recognize a great variety of tumor-associated antigens. Like with conventional monoclonal antibodies, each BiTE antibody shows very specific characteristics. Current BiTE candidates in development have been selected to fulfill high pharmaceutical standards for biologicals.



Online: PEGSummitEurope.com



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12:00 Improving the *in vivo* Utility of Targeted Toxins by Rendering them Bispecific

Daniel A. Vallera, Ph.D., Lion Scholar and Director, Section on Molecular Cancer Therapeutics, Professor of Therapeutic Radiology, University of Minnesota Cancer Center

Our research group focuses on the problems that have limited the development of a class of biological drugs known as targeted toxins in order to develop more effective anti-carcinoma therapeutic. Using genetic engineering, we have found that simultaneously targeting certain overexpressed tumor markers with dual ligands results in a more potent and efficacious drug. Since the anti-toxin response of the patient has been shown to reduce drug effectiveness, we also concentrated our efforts on mutating toxin in order to reduce serum anti-toxin levels. The results are new drugs that are highly effective in human xenograft models.

12:30 Lunch for Purchase in the Exhibit Hall

13:45 Dedicated Poster Viewing in the Exhibit Hall

Engineering for Enhanced Stability and Manufacturability of Proteins

14:30 Chairperson's Remarks

Bernhardt L. Trout, Ph.D., MIT

14:35 KEYNOTE PRESENTATION

Incorporation of Developability and Manufacturability in Therapeutic Antibody Discovery



Bernhardt L. Trout, Ph.D., Director, Novartis-MIT Center for Continuous Manufacturing; Director, Concourse; Co-Chair, Singapore-MIT Alliance, Chemical and Pharmaceutical Engineering; Professor, Department of Chemical Engineering, MIT

We describe a new strategic approach to the formulation and stabilization of biotherapeutics. The approach is based on applying both molecular and macroscopic modeling tools in order to gain an understanding of degradation processes with unprecedented detail and accuracy. This approach allows the rational inclusion of screening molecules for developability and manufacturability during discovery, identifying key sites that are responsible for degradation for the purpose of removing them, identifying sites for conjugation of payloads, and identifying binding regions.

15:05 *In Silico* Methods to Reduce Development Risks in Biotherapeutics: Engineering Optimal Lead Compounds

Jesús Zurdo, Ph.D., Head of Innovation, LCM Development Services, Lonza Biologics plc

Protein aggregation and low stability imposes severe restraints in the development of biopharmaceuticals, potentially increasing the risks of undesired immune responses in patients. Predictive algorithms can be used to re-designing therapeutic antibodies with improved stability properties.

15:35 Refreshment Break

16:00 Sponsored Presentation (Opportunity Available)

16:30 Screening Antibody Candidates for Manufacturability, Stability, and Deliverability

Andrew Kosky, Senior Manager, Early Stage Pharmaceutical Development, Genentech, Inc.

Monoclonal antibodies can be difficult to manufacture, stabilize, and administer to patients in a convenient format; this is especially the case for therapeutic agents that require high doses and subcutaneous delivery. The intrinsic physicochemical properties that govern the manufacturability and deliverability of these molecules can be difficult to predict from primary sequence. The focus of this talk is a screening strategy that is designed to rapidly and accurately assess the manufacturability, stability, and deliverability of therapeutic antibody candidates. Data from the screening studies can be used to inform the candidate selection process.

17:00 Engineered Ig-Like Bispecific Molecules with Enhanced Therapeutic Potential

Justin Caravella, Ph.D., Scientist, Physical Biochemistry, Drug Discovery, Biogen Idec, Inc.

Stabilized single chain Fv fragments are building blocks for constructing Ig-like bispecific antibodies. Focused engineering platform technology for stabilizing single chain Fv fragments will be discussed, as well as characterization of Ig-like bispecific molecules.

17:30 Close of Conference



Difficult Protein Expression and Purification

6-7 October

WEDNESDAY, 6 OCTOBER

13:00 Conference Registration

Problem Protein Solutions

14:00 Chairperson's Remarks

Kenneth Lundstrom, Ph.D., CEO, PanTherapeutics

14:05 Cell-Free Production of Difficult Pharmaceutical Targets: Case Studies of G-Protein Coupled Receptors and Alzheimer's Disease Related Proteins

Frank Bernhard, Ph.D., Centre for Biomolecular Magnetic Resonance, Institute for Biophysical Chemistry, University of Frankfurt/Main

Cell-free expression eliminates major bottlenecks in the synthesis of membrane proteins and allows their production in completely new modes. We exemplify protocol development strategies for the efficient production of GPCRs in individual cell-free systems. We further demonstrate the high quality production of the Endothelin receptor, the major player in blood pressure regulation, and we present structural data of cell-free produced subunits of the γ -secretase complex.

14:35 Semliki Forest Virus Vectors: Versatile Tools for Protein Production

Kenneth Lundstrom, Ph.D., CEO, PanTherapeutics

Recombinant protein production is an essential part of modern biotechnology. Semliki Forest virus (SFV) vectors have been applied for protein production in drug development and structural biology and in neuroscience and gene therapy. SFV is particularly useful for the expression of difficult proteins such as membrane receptors. Rapid high-titer virus production, broad host range, high levels of transient gene expression are attractive features of SFV.

15:05 High-Level Production and Characterization of a G-Protein Coupled Receptor Signaling Complex

Stephen Marino, Ph.D., Department of Molecular Membrane Biology, Max Planck Institute of Biophysics

The presentation describes the combination of factors permitting the successful overproduction of a physiologically relevant G protein-coupled receptor (GPCR) complex. An evaluation of these factors (generalizable for other receptors), their advantages and disadvantages, as well as demonstration of the functionality of the resulting receptor species, will be discussed.

15:35 Coffee Break

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16:00 Advancing Synthetic Gene Design

Claes Gustafsson, Ph.D., Vice President, Marketing and Sales, DNA2.0

Gene synthesis offers immense flexibility in the tailoring of genes for practical uses. Capturing the value of this flexibility, however, is greatly limited by lack of understanding of the interactions between gene sequence features and host expression systems. DNA2.0 has developed a novel approach to interrogate the gene design preferences of expression hosts to maximize production from synthetic genes. Applications of this approach for a number of target proteins in several different host organisms will be discussed.

16:15 An Accelerated Protein Stability Testing Assay For Optimizing Purification Steps and Storage Conditions

Sponsored by



Wayne F. Patton, Ph.D., Chief Scientific Officer, Enzo Life Sciences

Aggregation tendency is often studied by exposing a protein solution to extreme conditions of temperature, pH, humidity, and light, referred to as forced photodegradation studies. Proteins degraded in this manner can reflect the degradation pathway(s) experienced during the product's lifetime. A rapid high-throughput fluorescence-based assay for assessing stability of monoclonal antibodies and recombinant therapeutic proteins is described. The ProteoStat® Thermal Shift Assay is performed using a temperature-regulated fluorimeter or a real-time PCR instrument. The assay is suitable for screening for protein stability as a function of pH, ionic strength, and concentration and the analysis of ligand binding.

16:30 A Simplified Protocol for the Refolding and Purification of Recombinant Human β -Secretase 1 (BACE1) Expressed in Escherichia coli for Structural Studies

Zhongren Wu, Research Fellow, Biochemistry, Vitae Pharmaceuticals

The BACE1 protein was prepared using a novel molecular construct designed using X-ray structures, in which a protease cleavage site is included for propeptide removal. The BACE1 protein is expressed in *E. coli* as inclusion bodies and refolding is accomplished in water without adding any "redox pair". Up to 50 mg highly purified, active BACE1 can be purified from one liter culture, under one week. The protein has been crystallized successfully.

17:00 EasyProt: An Innovative Protein Expression System Based on the Secretion System Type III of Pseudomonas aeruginosa

Audrey Le Gouellec, Ph.D., Assistante Hospitalo-Universitaire, HumProTher Lab, Joseph Fourier University

We present a technology to produce recombinant proteins using *P. aeruginosa* strain. The type III secretion system is used to secrete into the medium the heterologous proteins produced, thus facilitating their purification and functional analysis. The secretion of proteins into the oxidative extracellular medium could favor natural folding and disulfide bridge formation. We used this technology to screen vaccine antigen for anti-tumoral immunotherapy.

18:30 – 21:00 BIOTECHNICA Night: Beer Hall, Full Dinner Reception, Live Band

(Please register to reserve your complimentary ticket ahead of time. No tickets will be available on-site.)

THURSDAY, 7 OCTOBER

9:00 Conference Registration and Morning Coffee

Automation and High-Throughput

9:30 Chairperson's Opening Remarks

9:35 Production of scFv Fragments on the G/L Scale in the Cytoplasm of E. coli

Dominique Desplancq, Ph.D., Research scientist, Biotechnologie des Interactions Moleculaires, Institut de Recherche de l'Ecole de Biotechnologie de Strasbourg

The overproduction of single chain Fv fragments in *E. coli* requires their secretion into the periplasm indispensable for the formation of the stabilizing intra-molecular disulfide bonds. We have constructed a large library of scFvs that are folded and active in the absence of disulfide bridge formation. Such scFvs were expressed by auto-induction in the cytoplasm of *E. coli* with yields in the order of gram per liter in shake flasks.

10:05 Parallel Protein Production and Verification of Protein Product Using a High-Throughput Method in Plate Format

Louise Yderland, Group Leader, Proteomics, School of Biotechnology, Royal Institute of Technology, Albanova Universitetscentrum

We present a fast and reliable screening method for parallel protein expression and verification, which will save time and money. Performing cultivations in plate format using EnBase Flo technique enables automatic sample handling and parallel cultivation of a large number of unique proteins. Due to the plate format design, each step requires minimal hands-on time. The EnBase Flo technique in 24-deep well plates was used to reduce culture volume and increase protein yield.

10:35 Coffee Break

Sponsored by



11:00 Sponsored Presentation (Opportunity Available)

11:30 Automated Multigene Recombineering for Protein Complex Production in Prokaryotic and Eukaryotic Hosts

Imre Berger, Ph.D., Group Leader, Berger Group, EMBL-Grenoble

The study of multiprotein complexes depends on recombinant expression. We developed MultiBac, a baculovirus/insect cell system for eukaryotic multiprotein production. Rapid revision of expressions and diversification of complexes requires automation. ACEMBL, our automated unrestricted system for protein complex expression uses recombineering to facilitate multigene assembly and diversification. We show protein complex expressions using our technologies, including the complete prokaryotic holotranslocon.

12:00 High-Throughput Technologies for Preparation of High Value Proteins

Gert E. Folkers, Ph.D., NMR Spectroscopy Research Group, Bijvoet Center for Biomolecular Research, Utrecht University

We implemented an automated small-scale expression screening procedure to clone eukaryotic protein domains and demonstrate that high-throughput technology permits expression of a large part of all domains of cytoplasmatic human gene products. From numerous screening experiments we identified several parameters including culture conditions, induction procedure, that were previously not considered to significantly contribute to protein expression in *E. coli*.

12:30 Lunch for Purchase in the Exhibit Hall

13:45 Dedicated Poster Viewing in the Exhibit Hall

Unique Proteins – Unique Techniques

14:30 Chairperson's Remarks

James Groarke, Ph.D., Senior Research Investigator II, Protein Structure, Novartis Institute for Biomedical Research

14:35 The Baculovirus Expression Platform: Recent Advances & More Lessons Learned

James Groarke, Ph.D., Senior Research Investigator II, Protein Structure, Novartis Institute for Biomedical Research

Topics will cover some recent cloning/expression technologies using the baculovirus platform. Real case examples of the utilization of these new technologies enabling the purification of difficult proteins.

15:05 A Simple High-Throughput Purification Method for Hit Identification in Protein Screening

Emma Cummins, MSc., Senior Scientist, Global Biotherapeutic Technologies, Pfizer

15:35 Refreshment Break

Polypeptide Expression

16:00 Sponsored Presentation (Opportunity Available)

16:30 Elastin-Like Polypeptides – Up-and-Coming Tools for Recombinant Protein Expression and Biomedical Application

Doreen M. Floss, Ph.D., Researcher, Institute of Biochemistry, Christian-Albrechts-University

Elastin-like polypeptides (ELPs) are highly biocompatible and exhibit a thermally responsive reversible phase transition improving the efficiency of recombinant protein purification and making them attractive for biomedical applications. ELPylation technology has been extended to plant cells, and a number of plant-based expression systems have been evaluated for the production of both biopharmaceuticals and industrial ELPylated proteins.

17:00 Secreted Production of an Elastin-Like Polypeptide by *Pichia pastoris*

Roelof Schipperus, M.S., Agrotechnology and Food Sciences Group, Wageningen University and Research Center

Elastin-like polypeptides are designer polypeptides designed after elastin, a fibrous protein providing vertebrate tissues with elasticity. Elastin-like polypeptides have a temperature response that is dependent on their amino acid composition and chain length, making them highly interesting candidates for the construction of biomaterials. We have studied their expression using *Pichia pastoris*, and established the first reported case of secreted expression of elastin-like polypeptides.

17:30 Close of Conference



HOTEL & TRAVEL INFORMATION

Conference Venue:
Hannover Exhibition Grounds
Deutsche Messe
Messegelände
30521 Hannover
GERMANY

Please go to the following website for general visitor info and to make a hotel reservation
<http://www.biotechnica.de/visitorservice>

ABOUT BIOTECHNICA

Geared to "Evolution of business and research" BIOTECHNICA 2010 invites you to Europe's leading gathering for biotechnology and life sciences, staged annually in Hannover, Germany. For three days the exhibition halls, the conference rooms and the Partnering meeting boxes will be alive with exhibitors and visiting professionals from all over the world, together with investors and distinguished speakers from business, science and politics - all here to discuss the latest products, innovations, research findings and market opportunities.

Maximize your sales prospects. From research and product development, equipment, process technology and services to production and marketing: the exhibition section of BIOTECHNICA charts the biotech industry's value-adding chain from start to finish. Alongside the big industry players and SMEs, which have their own stands at the show, young and emerging biotech firms and scientific establishments are given ideal opportunities to showcase their work at the many group display stands representing national and international BioClusters and industry associations.

Reduce time and cost by making BIOTECHNICA the event of your choice in 2010. You can close deals, find business or research partners, discuss politics and forms of financing with experts and meet old and new friends - all this under one roof in just three days! All details at www.biotechnica.de.

Your conference registration includes access to the BIOTECHNICA Exhibition Hall!

SPONSORSHIP AND EXHIBIT INFORMATION

Whether you are ready to present an exciting new technology, preparing for a new product launch, or need feedback on a specific idea, PEGS Europe offers the perfect platform for you to present to a high-level, targeted audience.

The Biotechnica exhibit hall will host **13,000 attendees** over the course of the event. Co-location with Biotechnica will allow you to exhibit as part of the larger event and reach your target audience in the PEGS Europe session rooms, with an expected attendance of 300 delegates.

Exhibit in the PEGS Pavilion in the Biotechnica hall, and you will be located in the central location for all PEGS delegates. Traffic-building programs will be in place to ensure delegates visit this pavilion.

Sponsors will get the opportunity to participate in three networking events offered to you free-of-charge by Biotechnica & CHI:

- Monday evening - pre-conference keynote presentation & reception
- Tuesday evening - PEGS attendees have an exclusive dinner reception held at the convention center within close proximity to the session rooms.
- Wednesday evening - a second social hosted by Biotechnica in the Bavarian Beer hall, complete with dinner and a traditional German band.

These receptions are an excellent opportunity to network with your target audience. Attendance is included in selected sponsorship packages.

Sponsorship Opportunities:

Podium Presentations

A 15- to 30-minute podium presentation as part of the main conference. (May also include a table-top in the foyer during the exclusive PEGS Tuesday evening dinner reception.)

Coffee Breaks (Exclusive per Break)

Coffee breaks will be held in close proximity of the conference sessions. Table-top will be available for sponsoring company to display corporate product literature.

Session Chair (Exclusive per Session)

An executive from your company will chair a session (a group of talks) on the main conference program. Includes a brief introduction to the entire session and the individual speakers.

Exhibitor Information

Exhibitors at PEGS Europe will enjoy facilitated networking opportunities with more than 300 high-level decision-makers. Speak face-to-face with prospective clients and showcase your latest product, service or solution.

Marketing support from CHI and Biotechnica will include

- Combined brochure mailings of 150,000
- Email campaigns of 1 million impressions

For more information on sponsorship and exhibit opportunities, please contact:

Carol Dinerstein
Director, Business Development
+1 781-972-5471
dinerstein@healthtech.com

HOW TO REGISTER:  **Online: PEGSummitEurope.com****Key Code 1009F****Email: reg@healthtech.com****Phone: +1-781-972-5400 Option 1****Fax: +1-781-972-5425****1. REGISTRATION INFORMATION** Mr. Ms. Mrs. Dr. Prof.

Name _____

Job Title _____ Div./Dept. _____

Company _____

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How would you prefer to receive notices from CHI? Email: Yes No Fax: Yes No

Email* _____ Fax _____

*Email is not a mandatory field. However, by excluding your email you will not receive notification about online access to pre-conference presenter materials, conference updates, networking opportunities and requested eNewsletters.

2. PRICING INFORMATION**SHORT COURSE PRICING**

	Commercial	Acad., Gov., Hospital-affiliated	Student
Protein Aggregation in Biopharmaceutical Products (14:00 -17:00)	<input type="checkbox"/> €495	<input type="checkbox"/> €295	<input type="checkbox"/> €125

EVENT PRICING

Advance Registration Deadline until 3 September	<input type="checkbox"/> €1595	<input type="checkbox"/> €755	<input type="checkbox"/> €450
Registrations after 3 September and on-site	<input type="checkbox"/> €1745	<input type="checkbox"/> €805	<input type="checkbox"/> €450

Please select the 2 conferences you're most likely to attend**5-6 October (Choose One)**

- Novel Antibody Constructs and Alternative Scaffolds
 Protein Expression and Cell Line Development

6-7 October (Choose One)

- Empowered Bispecific Antibodies
 Difficult Protein Expression and Purification

INDIVIDUAL CONFERENCE PRICING

Advance Registration Deadline until 3 September	<input type="checkbox"/> €1095	<input type="checkbox"/> €545	<input type="checkbox"/> €300
Registrations after 3 September and on-site	<input type="checkbox"/> €1245	<input type="checkbox"/> €625	<input type="checkbox"/> €300

Please select one conference**5-6 October**

- Novel Antibody Constructs and Alternative Scaffolds
 Protein Expression and Cell Line Development

6-7 October

- Empowered Bispecific Antibodies
 Difficult Protein Expression and Purification

COMPLIMENTARY BIOTECHNICA EVENTS**REQUIRED if you wish to attend these complimentary events.****TICKETS NOT AVAILABLE ON-SITE – PRE-REGISTRATION IS REQUIRED.**

- Monday, 4 October - BIOTECHNICA Opening and EUROPEAN BIOTECHNICA AWARD Ceremony plus Reception
 Wednesday, 6 October - BIOTECHNICA Night – Original Bavarian Beer Hall, full dinner reception, and band

DISCOUNTS

Poster Discount	<input type="checkbox"/> €35 off	<input type="checkbox"/> €35 off	<input type="checkbox"/> €35 off
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REGISTER 3 - 4th IS FREE

Individuals must register for the same conference or conference combination and submit completed registration form together for discount to apply. Please reproduce this registration form as needed.

GROUP DISCOUNTS AVAILABLE! Special rates are available for multiple attendees from the same organization.For more information on group discounts contact **David Cunningham at +1-781-972-5472**

- Please send me information on BIOTECHNICA's Partnering, an online networking tool
 I cannot attend but would like to purchase the PEGS Europe conference CD for €600 (plus shipping). Massachusetts delivery will include sales tax.

3. PAYMENT INFORMATION

- Enclosed is a check or money order payable to Cambridge Healthtech Institute, drawn on a U.S. bank, in U.S. currency.
 Invoice me, but reserve my space with credit card information listed below.

Invoices unpaid two weeks prior to conference will be billed to credit card at full registration rate. Invoices must be paid in full and checks received by the deadline date to retain registration discount. If you plan to register on site, please check with CHI beforehand for space availability.

Please charge: Visa (13-16 digits) MasterCard (16 digits)

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Present a Poster and Save €35!

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions.

To secure a poster board and inclusion in the conference materials, your abstract must be submitted, approved and your registration paid in full by **1:00 pm EDT, 8 September, 2010**. Register online, or by phone, fax or mail. Indicate that you would like to present a poster and you will receive abstract submission instructions via email.

I am interested in presenting a poster at

 PEGS Europe

Title _____

CHI Insight Pharma Reports

A series of diverse reports designed to keep life science professionals informed of the salient trends in pharmaceutical technology, business, clinical development, and therapeutic disease markets. For a detailed list of reports, visit

InsightPharmaReports.com, or contact Rose LaRaia, rlaraia@healthtech.com, +1-781-972-5444.

Barnett Educational Services

Barnett is a recognized leader in clinical education, training, and reference guides for life science professionals involved in the drug development process. For more information, visit www.barnettinternational.com.

Additional Registration Details

Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link.

 **Handicapped Equal Access**

In accordance with the ADA, Cambridge Healthtech Institute is pleased to arrange special accommodations for attendees with special needs. All requests for such assistance must be submitted in writing to CHI at least 30 days prior to the start of the meeting.

Substitution/Cancellation Policy

In the event that you need to cancel a registration, you may:

- Transfer your registration to a colleague within your organization. Credit your registration to another Cambridge Healthtech Institute program.
- Request a refund minus a €75 processing fee per conference.
- Request a refund minus the cost (€600) of ordering a copy of the CD.

NOTE: Cancellations will only be accepted up to two weeks prior to the conference.

Program and speakers are subject to change.

Video and or audio recording of any kind is prohibited onsite at all CHI events.